=> fil_reg; d que 18

FILE 'REGISTRY' ENTERED AT 16:10:51 ON 27 DEC 2004

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 26 DEC 2004 HIGHEST RN 802853-20-9 DICTIONARY FILE UPDATES: 26 DEC 2004 HIGHEST RN 802853-20-9

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at: http://www.cas.org/ONLINE/DBSS/registryss.html

L7

462 SEA FILE=REGISTRY ABB=ON ((H[AVSG][DE][GD][STV][FYN][STA][DSLN [EDL] [MIDVF] [NSQR] [TKYSV] [VIYMA] [LA] [DQK] [NTSDHRI] [LIMQFK] [AIS] [ATE] [RKWQ] [DELN] [FYE] [ILVK] [NKSLQED] [WN] [LVSI] [ILKMN] [QSNATDH] [TGSQ] [KRGFQ] [IVGTRE])) | ((H[AVSG] [DE] [GD] [STV] [FYN] [STA] [DSLN] [EDL] [MIDVF] [NSQR] [TKYSV] [VIYMA] [LA] [DQK] [NTSDHRI] [LIMQFK] [AIS] [ATE] [RKWQ] [DELN] [FYE] [ILVK] [NKSLQED] [WN] [LVSI] [ILKMN] [QSNATDH] [TGSQ] [KRGFQ] [IVGTRE]))T[DEQ] | ((H[AVSG] [DE] [GD] [STV] [FYN] [STA] [DSLN] [EDL] [MIDVF] [NSQR] [TKYSV] [VIYMA] [LA] [DQK] [NTSDHRI] [LIMQFK] [AIS] [ATE] [RKWQ] [DELN] [FYE] [ILVK] [NKSLQED] [WN] [LVSI] [ILKMN] [QSN ATDH] [TGSQ] [KRGFQ] [IVGTRE]))G ((H[AVSG] [DE] [GD] [STV] [FYN] [STA] [DSLN] [EDL] [MIDVF] [NSQR] [TKYSV] [VIYMA] [LA] [DQK] [NTSDHRI] [LIMQFK] [AIS] [ATE] [RKWQ] [DELN] [FYE] [ILVK] [NKSLQED] [WN] [LVSI] [ILKMN] [QSN ATDH] [TGSQ] [KRGFQ] [IVGTRE])) KE | ((H[AVSG] [DE] [GD] [STV] [FYN] [STA] [DSLN] [EDL] [MIDVF] [NSQR] [TKYSV] [VIYMA] [LA] [DQK] [NTSDHRI] [LIMQFK [AIS] [ATE] [RKWQ] [DELN] [FYE] [ILVK] [NKSLQED] [WN] [LVSI] [ILKMN] [QS NATDH] [TGSQ] [KRGFQ] [IVGTRE]))TDRK|((H[AVSG] [DE] [GD] [STV] [FYN] [S TA] [DSLN] [EDL] [MIDVF] [NSQR] [TKYSV] [VIYMA] [LA] [DQK] [NTSDHRI] [LIM QFK] [AIS] [ATE] [RKWQ] [DELN] [FYE] [ILVK] [NKSLQED] [WN] [LVSI] [ILKMN] [QSNATDH] [TGSQ] [KRGFQ] [IVGTRE]))SGKSD/SQSP

387-SEA-FILE=REGISTRY-ABB=ON-L7 AND 31-36/SQL

=> fil capl; d que 121; d que 119; d que 130; s 121 or 119 or 130 FILE CAPLUS TENTERED AT 16:11:07 ON 27 DEC 2004

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FILE COVERS 1907 - 27 Dec 2004 VOL 142 ISS 1 FILE LAST UPDATED: 24 Dec 2004 (20041224/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

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L7
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                  ] [ATE] [RKWQ] [DELN] [FYE] [ILVK] [NKSLQED] [WN] [LVSI] [ILKMN] [QSNATDH
                  ] [TGSQ] [KRGFQ] [IVGTRE])) | ((H[AVSG] [DE] [GD] [STV] [FYN] [STA] [DSLN]
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                  [ATE] [RKWQ] [DELN] [FYE] [ILVK] [NKSLQED] [WN] [LVSI] [ILKMN] [QSNATDH]
                  [TGSQ] [KRGFQ] [IVGTRE]))T [DEQ] | ((H[AVSG] [DE] [GD] [STV] [FYN] [STA] [
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                  [AIS] [ATE] [RKWQ] [DELN] [FYE] [ILVK] [NKSLQED] [WN] [LVSI] [ILKMN] [QSN
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                  [DSLN] [EDL] [MIDVF] [NSQR] [TKYSV] [VIYMA] [LA] [DQK] [NTSDHRI] [LIMQFK
                  ] [AIS] [ATE] [RKWQ] [DELN] [FYE] [ILVK] [NKSLQED] [WN] [LVSI] [ILKMN] [QS
                  NATDH] [TGSQ] [KRGFQ] [IVGTRE]))TDRK | ((H[AVSG] [DE] [GD] [STV] [FYN] [S
                  TA] [DSLN] [EDL] [MIDVF] [NSQR] [TKYSV] [VIYMA] [LA] [DQK] [NTSDHRI] [LIM
                  QFK] [AIS] [ATE] [RKWQ] [DELN] [FYE] [ILVK] [NKSLQED] [WN] [LVSI] [ILKMN]
                  [QSNATDH] [TGSQ] [KRGFQ] [IVGTRE]))SGKSD/SQSP
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L8 387 SEA FILE=REGISTRY ABB=ON L7 AND 31-36/SQL
L10 84 SEA FILE=CAPLUS ABB=ON L8
L12 20789 SEA FILE=CAPLUS ABB=ON GASTROINTESTIN?/OBI
L14 35924 SEA FILE=CAPLUS ABB=ON DIGESTIVE TRACT/CT
L15 132377 SEA FILE=CAPLUS ABB=ON INTESTINE/CT
L16 60379 SEA FILE=CAPLUS ABB=ON STOMACH/CT
L20 25 SEA FILE=CAPLUS ABB=ON L10(L)(THU OR PAC OR PKT OR DMA

Roles THM- therapeutic use

L20 25 SEA FILE=CAPLUS ABB=ON L10(L) (THU OR PAC OR PKT OR DMA)/RL PAC-pharmacologic L21 22 SEA FILE=CAPLUS ABB=ON L20 AND (F12 OR L14 OR L15 OR L16))

PKT- pharmacokinetics

> DMA deng mechanism of action

L7

L8

462 SEA FILE=REGISTRY ABB=ON ((H[AVSG] [DE] [GD] [STV] [FYN] [STA] [DSLN [EDL] [MIDVF] [NSQR] [TKYSV] [VIYMA] [LA] [DQK] [NTSDHRI] [LIMQFK] [AIS [ATE] [RKWQ] [DELN] [FYE] [ILVK] [NKSLQED] [WN] [LVSI] [ILKMN] [QSNATDH] [TGSQ] [KRGFQ] [IVGTRE])) | ((H[AVSG] [DE] [GD] [STV] [FYN] [STA] [DSLN] [EDL] [MIDVF] [NSQR] [TKYSV] [VIYMA] [LA] [DQK] [NTSDHRI] [LIMQFK] [AIS] [ATE] [RKWQ] [DELN] [FYE] [ILVK] [NKSLQED] [WN] [LVSI] [ILKMN] [QSNATDH] [TGSQ] [KRGFQ] [IVGTRE]))T[DEQ] | ((H[AVSG] [DE] [GD] [STV] [FYN] [STA] [DSLN] [EDL] [MIDVF] [NSQR] [TKYSV] [VIYMA] [LA] [DQK] [NTSDHRI] [LIMQFK] [AIS] [ATE] [RKWQ] [DELN] [FYE] [ILVK] [NKSLQED] [WN] [LVSI] [ILKMN] [QSN DSLN] [EDL] [MIDVF] [NSQR] [TKYSV] [VIYMA] [LA] [DQK] [NTSDHRI] [LIMQFK] [AIS] [ATE] [RKWQ] [DELN] [FYE] [ILVK] [NKSLQED] [WN] [LVSI] [ILKMN] [QSN ATDH] [TGSQ] [KRGFQ] [IVGTRE])) KE | ((H[AVSG] [DE] [GD] [STV] [FYN] [STA] [DSLN] [EDL] [MIDVF] [NSQR] [TKYSV] [VIYMA] [LA] [DQK] [NTSDHRI] [LIMQFK [AIS] [ATE] [RKWQ] [DELN] [FYE] [ILVK] [NKSLQED] [WN] [LVSI] [ILKMN] [QS NATDH] [TGSQ] [KRGFQ] [IVGTRE]))TDRK ((H[AVSG] [DE] [GD] [STV] [FYN] [S TA] [DSLN] [EDL] [MIDVF] [NSQR] [TKYSV] [VIYMA] [LA] [DQK] [NTSDHRI] [LIM QFK] [AIS] [ATE] [RKWQ] [DELN] [FYE] [ILVK] [NKSLQED] [WN] [LVSI] [ILKMN] [QSNATDH] [TGSQ] [KRGFQ] [IVGTRE]))SGKSD/SQSP

387 SEA FILE=REGISTRY ABB=ON L7 AND 31-36/SQL

L10 84 SEA FILE=CAPLUS ABB=ON L8

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L12 20789 SEA FILE=CAPLUS ABB=ON GASTROINTESTIN?/OBI
L14 35924 SEA FILE=CAPLUS ABB=ON DIGESTIVE TRACT/CT
L15 132377 SEA FILE=CAPLUS ABB=ON INTESTINE/CT
L16 60379 SEA FILE=CAPLUS ABB=ON STOMACH/CT
L18 36198 SEA FILE=CAPLUS ABB=ON (L12 OR (L14 OR L15 OR L16))(L)(DISEASE #/OBI OR DISORDER#/OBI OR INFLAMM?/OBI)
L19 21 SEA FILE=CAPLUS ABB=ON L18 AND L10
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L7 462 SEA FILE=REGISTRY ABB=ON ((H[AVSG][DE][GD][STV][FYN][STA][DSLN [EDL] [MIDVF] [NSQR] [TKYSV] [VIYMA] [LA] [DQK] [NTSDHRI] [LIMOFK] [AIS] [ATE] [RKWQ] [DELN] [FYE] [ILVK] [NKSLQED] [WN] [LVSI] [ILKMN] [QSNATDH] [TGSQ] [KRGFQ] [IVGTRE])) | ((H[AVSG] [DE] [GD] [STV] [FYN] [STA] [DSLN] [EDL] [MIDVF] [NSQR] [TKYSV] [VIYMA] [LA] [DQK] [NTSDHRI] [LIMQFK] [AIS] [ATE] [RKWQ] [DELN] [FYE] [ILVK] [NKSLQED] [WN] [LVSI] [ILKMN] [QSNATDH] [TGSQ][KRGFQ][IVGTRE]))T[DEQ] | ((H[AVSG][DE][GD][STV][FYN][STA][DSLN] [EDL] [MIDVF] [NSQR] [TKYSV] [VIYMA] [LA] [DQK] [NTSDHRI] [LIMQFK] [AIS] [ATE] [RKWQ] [DELN] [FYE] [ILVK] [NKSLQED] [WN] [LVSI] [ILKMN] [QSN ATDH] [TGSQ] [KRGFQ] [IVGTRE]))G| ((H[AVSG] [DE] [GD] [STV] [FYN] [STA] [DSLN] [EDL] [MIDVF] [NSQR] [TKYSV] [VIYMA] [LA] [DQK] [NTSDHRI] [LIMQFK] [AIS] [ATE] [RKWQ] [DELN] [FYE] [ILVK] [NKSLQED] [WN] [LVSI] [ILKMN] [QSN ATDH] [TGSQ] [KRGFQ] [IVGTRE])) KE | ((H[AVSG] [DE] [GD] [STV] [FYN] [STA] [DSLN] [EDL] [MIDVF] [NSQR] [TKYSV] [VIYMA] [LA] [DQK] [NTSDHRI] [LIMQFK] [AIS] [ATE] [RKWQ] [DELN] [FYE] [ILVK] [NKSLQED] [WN] [LVSI] [ILKMN] [QS NATDH] [TGSQ] [KRGFQ] [IVGTRE])) TDRK | ((H[AVSG] [DE] [GD] [STV] [FYN] [S TA] [DSLN] [EDL] [MIDVF] [NSQR] [TKYSV] [VIYMA] [LA] [DQK] [NTSDHRI] [LIM QFK] [AIS] [ATE] [RKWQ] [DELN] [FYE] [ILVK] [NKSLQED] [WN] [LVSI] [ILKMN] [QSNATDH] [TGSQ] [KRGFQ] [IVGTRE]))SGKSD/SQSP

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L45 26 L21 OR L19 OR L30
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=> fil uspatf; d que 144
FILE USPATFULL DENTERED AT 16:11:13 ON 27 DEC 2004
CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)
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FILE COVERS 1971 TO PATENT PUBLICATION DATE: 23 Dec 2004 (20041223/PD)
FILE LAST UPDATED: 23 Dec 2004 (20041223/ED)
HIGHEST GRANTED PATENT NUMBER: US6834393
HIGHEST APPLICATION PUBLICATION NUMBER: US2004261151
CA INDEXING IS CURRENT THROUGH 23 Dec 2004 (20041223/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 23 Dec 2004 (20041223/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Oct 2004
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Oct 2004

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USPAT2 is now available. USPATFULL contains full text of the
>>>
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     original, i.e., the earliest published granted patents or
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    applications. USPAT2 contains full text of the latest US
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    publications, starting in 2001, for the inventions covered in
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    USPATFULL. A USPATFULL record contains not only the original
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    published document but also a list of any subsequent
                                                                       <<<
    publications. The publication number, patent kind code, and
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>>> publication date for all the US publications for an invention
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    are displayed in the PI (Patent Information) field of USPATFULL
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    records and may be searched in standard search fields, e.g., /PN,
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    /PK, etc.
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    USPATFULL and USPAT2 can be accessed and searched together
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     through the new cluster USPATALL. Type FILE USPATALL to
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     enter this cluster.
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    Use USPATALL when searching terms such as patent assignees,
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    classifications, or claims, that may potentially change from
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    the earliest to the latest publication.
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This file contains CAS Registry Numbers for easy and accurate substance identification.

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L7
             462 SEA FILE=REGISTRY ABB=ON ((H[AVSG][DE][GD][STV][FYN][STA][DSLN
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L8
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L33
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L34
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L36
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L38
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L39
                 OR L38)
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L43
L44
          14 SEA FILE USPATFULL ABB ON L39 NOT L43
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=>=dup=rem=145,144

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FILE 'USPATFULL' ENTERED AT 16:11:20 ON 27 DEC 2004
CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)
PROCESSING COMPLETED FOR L45
PROCESSING COMPLETED FOR L44
L46
3'8 DUP REM L45 L44 (2 DUPLICATES REMOVED)

ANSWERS '1-26' FROM FILE CAPLUS ANSWERS '27-38' FROM FILE USPATFULL

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L46 ANSWER 1 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1
ACCESSION NUMBER:
                          2004:219841 CAPLUS
DOCUMENT NUMBER:
                          140:247608
                          Pharmaceutical compositions and methods for the use of
TITLE:
                          GLP analogs in the treatment, prevention, diagnosis,
                          and prognosis of bone-related and nutrition-related
                          disorders
                          Henriksen, Dennis B.; Holst, Jens J.
INVENTOR(S):
PATENT ASSIGNEE(S):
                          Den.
                          U.S. Pat. Appl. Publ., 50 pp., Cont.-in-part of U.S.
SOURCE:
                          Pat. Appl. 2002 37,836.
                          CODEN: USXXCO
DOCUMENT TYPE:
                          Patent
                          English
LANGUAGE:
                                                                            print the
Registry
-- sequence
20
18 record for
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
                          KIND
                                 DATE
                                             APPLICATION NO.
                                                                     DATE
     PATENT NO.
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                                                                      _____
     ______
                                                                     20030320
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                                                                                Registry
numbers
because there
were many &
if is expensive
                                                                     20010918
                                 20040506
                                             EP 2001-967517
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     EP 1414486
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             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
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                                                                  A 20000918
PRIORITY APPLN. INFO.:
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                                              GB 2000-29920
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                                                                  A2 20010918
                                              US 2002-371307P
                                                                  P 20020410
                                              WO 2001-GB4178
                                                                  W 20010918
                          MARPAT 140:247608
                                                                                 to do 50.
OTHER SOURCE(S):
     Entered STN: 19 Mar 2004
                                                                                   If a you
     The present invention relates to methods for prevention and treatment of
AB
     bone-related or nutrition-related disorders using a GLP mol. or GLP
                                                                                  find one or
     activator either alone or in combination with another therapeutic.
     present invention also encompasses methods of diagnosing or monitoring the more and les
     progression of a disorder. The invention also encompasses methods of
                                                                                  of interest,
     monitoring the effectiveness of treatment of the invention.
                                                                            I can display
the Registry
records for
IC
     ICM A61K038-26
     ICS A61K031-66; A61K031-56; A61K033-24
     424617000; 514008000; 514171000; 514012000; 514102000
NCL
     2-6 (Mammalian Hormones)
IT
     Nutrition, animal
                                                                                     those
        (disorders; pharmaceutical compns. and methods for use of glucagon-like
                                                                                     articles
        peptides (GLP) analogs in treatment, prevention, diagnosis, and
        prognosis of bone-related and nutrition-related disorders)
IT
     Anorexia
     Bone, disease
     Cardiovascular system, disease
     Diabetes mellitus
     Diagnosis
     Drug delivery systems
     Hyperparathyroidism
```

Hypertension Nutrients Obesity

Osteomalacia Osteoporosis

Periodontium, disease

Prognosis

(pharmaceutical compns. and methods for use of glucagon-like peptides (GLP) analogs in treatment, prevention, diagnosis, and prognosis of bone-related and nutrition-related disorders)

IT 671252-45-2

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(pharmaceutical compns. and methods for use of glucagon-like peptides (GLP) analogs in treatment, prevention, diagnosis, and prognosis of bone-related and nutrition-related disorders')

IT 671255-70-2 671255-72-4 671255-73-5 671255-74-6.671255-75-7

671255-76-8 671255-78-0 671255-79-1 671255-80-4

671255-81-5 671255-82-6

RL: PRP (Properties)

(unclaimed protein sequence; pharmaceutical compns. and methods for the use of GLP analogs in the treatment, prevention, diagnosis, and prognosis of bone-related and nutrition-related disorders)

=> d ibib ed ab hitind 2-38

L46 ANSWER 2 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 2

ACCESSION NUMBER:

2001:719082 CAPLUS

DOCUMENT NUMBER: TITLE:

135:267701

Large intestine function enhancement and intestinal inflammatory disease treatment using glucagon-like

peptide 2 and GLP-2 analogs

INVENTOR(S):

Drucker, Daniel J.

PATENT ASSIGNEE(S):

1149336 Ontario, Inc., Can.

SOURCE:

U.S., 17 pp., Cont.-in-part of U.S. Ser. No. 850,664,

abandoned.
CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|-------------|
| | | | | |
| US 6297214 | B1 | 20011002 | US 1998-149831 | 19980908 |
| US 6586399 | B1 | 20030701 | US 2000-692238 | 20001020 |
| US 2003207809 | A1 | 20031106 | US 2003-419150 | 20030421 |
| PRIORITY APPLN. INFO.: | | | US 1997-850664 | B2 19970502 |
| | | | US 1998-149831 | A1 19980908 |
| | | | US 2000-692238 | A3 20001020 |

ED Entered STN: 03 Oct 2001

AB The invention relates to glucagon-related peptides and their use for the prevention or treatment of disorders involving the large intestine. In particular, it has now been demonstrated that GLP-2 and peptidic agonists of GLP-2 can cause proliferation of the tissue of large intestine. Thus, the invention provides methods of proliferating the large intestine in a subject in need thereof. Further, the methods of the invention are useful to treat or prevent inflammatory conditions of the large intestine, including inflammatory bowel diseases. Also claimed are methods for identifying other peptides useful in treating inflammatory conditions

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involving the large intestine.
IC
     ICM A61K038-00
NCL
     514012000
     2-6 (Mammalian Hormones)
CC
     Section cross-reference(s): 1, 14
TT
     Intestine, disease
        (Crohn's; large intestine function enhancement and intestinal
        inflammatory disease treatment using glucagon-like
        peptide 2 and GLP-2 analogs)
     Intestine, disease
IT
        (colitis, infectious and drug- or chemical-induced; large intestine
        function enhancement and intestinal inflammatory
        disease treatment using glucagon-like peptide 2 and GLP-2
        analogs)
IT
     Intestine, disease
        (colitis, ischemic; large intestine function enhancement and intestinal
        inflammatory disease treatment using glucagon-like
        peptide 2 and GLP-2 analogs)
     Intestine, disease
TT
        (diverticulitis; large intestine function enhancement and intestinal
        inflammatory disease treatment using glucagon-like
        peptide 2 and GLP-2 analogs)
IT
     Intestine, disease
        (inflammatory; large intestine function enhancement and
        intestinal inflammatory disease treatment using
        glucagon-like peptide 2 and GLP-2 analogs)
IT
     Intestine
        (large; large intestine function enhancement and intestinal
        inflammatory disease treatment using glucagon-like
        peptide 2 and GLP-2 analogs)
IT
     Intestine
        (mucosa; large intestine function enhancement and intestinal
        inflammatory disease treatment using glucagon-like
        peptide 2 and GLP-2 analogs)
IT
     Intestine
        (resection, partial or subtotal large intestine; large intestine
        function enhancement and intestinal inflammatory
        disease treatment using glucagon-like peptide 2 and GLP-2
        analogs)
IT
     Intestine, disease
        (ulcerative colitis; large intestine function enhancement and
        intestinal inflammatory disease treatment using
        glucagon-like peptide 2 and GLP-2 analogs)
     89750-15-2, glucagon-like peptide 2
                                            89750-15-2D, glucagon-like peptide
TT
     2, analogs 195262-56-7 197664-29-2 197922-42-2
     197922-60-4 197923-49-2 223460-79-5,
     1-33-Glucagon-like peptide II (human)
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (large intestine function enhancement and intestinal inflammatory
        disease treatment using glucagon-like peptide 2 and GLP-2 analogs)
                               THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS
REFERENCE COUNT:
                         39
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
L46 ANSWER 3 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN
                         2004:996119 CAPLUS
ACCESSION NUMBER:
DOCUMENT NUMBER:
                         141:406152
TITLE:
                         Glutaminyl-based dipeptidyl peptidase IV (DPIV)
                         inhibitors, pharmaceutical compositions, and use
INVENTOR(S):
                         Demuth, Hans-Ulrich; Hoffmann, Matthias; Hoffmann,
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Torsten; Niestroj, Andre J.; Schilling, Stephan;

Heiser, Ulrich Prosidion Ltd., UK PATENT ASSIGNEE(S): SOURCE: PCT Int. Appl., 497 pp. CODEN: PIXXD2 DOCUMENT TYPE: Patent English LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION: PATENT NO. KIND DATE APPLICATION NO. DATE ------------------------WO 2004-EP4774 20040505 WO 2004099134 A2 20041118 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG US 2004229848 20041118 Δ1 US 2004-839122 20040505 PRIORITY APPLN. INFO.: US 2003-467914P P 20030505 US 2003-468014P P 20030505 ED Entered STN: 19 Nov 2004 The invention discloses dipeptidyl peptidase IV (DPIV) inhibitors, more particularly, glutaminyl derivs., wherein the glutamine residue is bound in a peptide manner to a moiety which imitates the amino acid residue proline, especially to a nitrogen containing moiety. The invention also discloses pharmaceutical compns. containing these compds., and the use of these compds. in inhibiting DPIV and DPIV-like enzyme activity. IC ICM C07D207-00 CC 1-12 (Pharmacology) Section cross-reference(s): 63 IT Intestine, disease (Crohn's; glutaminyl-based dipeptidyl peptidase IV (DPIV) inhibitors, pharmaceutical compns., and use) IT Gastrointestinal hormone receptors RL: BSU (Biological study, unclassified); BIOL (Biological study) (gastric inhibitory polypeptide, agonists; glutaminyl-based dipeptidyl peptidase IV (DPIV) inhibitors, pharmaceutical compns., and use) IT Drugs (gastrointestinal; glutaminyl-based dipeptidyl peptidase IV (DPIV) inhibitors, pharmaceutical compns., and use) TT Intestine, disease

IT Intestine, disease
 (inflammatory:

(inflammatory; glutaminyl-based dipeptidyl peptidase IV (DPIV) inhibitors, pharmaceutical compns., and use)

IT Intestine, disease

(ulcerative colitis; glutaminyl-based dipeptidyl peptidase IV (DPIV) inhibitors, pharmaceutical compns., and use)

IT 56-03-1D, Biguanide, derivs. 56-85-9D, Glutamine, derivs. 59-67-6,
Nicotinic acid, biological studies 100-55-0, Nicotinyl alcohol
657-24-9, Metformin 56180-94-0, Acarbose 141758-74-9, AC-2993
197922-42-2, ALX-0600 204656-20-2, NN-2211

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(glutaminyl-based dipeptidyl peptidase IV (DPIV) inhibitors, pharmaceutical compns., and use)

L46 ANSWER 4 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN

Harle 10/042746 Page 9

ACCESSION NUMBER: 2004:817916 CAPLUS DOCUMENT NUMBER: 141:326195 TITLE:

Synthesis of protracted GLP-2 derivatives attached to

an hydrophilic substituent and therapeutic uses

thereof

INVENTOR (S): Kodra, Janos Tibor; Johansen, Nils Langeland; Thim,

Lars; Peschke, Bernd

PATENT ASSIGNEE(S): Novo Nordisk A/S, Den. PCT Int. Appl., 66 pp. SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE: Patent English LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

| PAT | CENT : | NO. | | | KIN | D 1 | DATE | | | APPL | ICAT | ION I | NO. | | D. | ATE | |
|-----|--------|------|-----|-----|-----|-----|------|------|-----|------|-------|-------|-----|-----|-----|------|--------------|
| | | | | | | - | | | | | | | | | - | | - |
| WO | 2004 | 0854 | 71 | | A2 | : | 2004 | 1007 | 1 | WO 2 | 004-1 | DK19 | 8 | | 2 | 0040 | 323 |
| WO | 2004 | 0854 | 71 | | A3 | : | 2004 | 1104 | | | | | | | | | |
| | W: | ΑE, | AG, | AL, | AM, | ΑT, | AU, | ΑZ, | BA, | BB, | BG, | BR, | BW, | BY, | ΒZ, | CA, | CH, |
| • | | CN, | CO, | CR, | CU, | CZ, | DE, | DK, | DM, | DZ, | EC, | EE, | EG, | ES, | FI, | GB, | GD, |
| | | GE, | GH, | GM, | HR, | HU, | ID, | IL, | IN, | IS, | JP, | KE, | KG, | ΚP, | KR, | ΚZ, | LC, |
| | | LK, | LR, | LS, | LT, | LU, | LV, | MA, | MD, | MG, | MK, | MN, | MW, | MX, | MZ, | NA, | NI, |
| | | NO, | NZ, | OM, | PG, | PH, | PL, | PT, | RO, | RU, | SC, | SD, | SE, | SG, | SK, | SL, | SY, |
| | | TJ, | TM, | TN, | TR, | TT, | TZ, | UA, | ŪĠ, | US, | UZ, | VC, | VN, | YU, | ZA, | ZM, | zw |
| | RW: | BW, | GH, | GM, | KE, | LS, | MW, | MZ, | SD, | SL, | SZ, | TZ, | UG, | ZM, | ZW, | AM, | ΑZ, |
| | | BY, | KG, | KZ, | MD, | RU, | ТJ, | TM, | AT, | BE, | BG, | CH, | CY, | CZ, | DE, | DK, | EE, |
| | | ES, | FI, | FR, | GB, | GR, | HU, | ΙE, | IT, | LU, | MC, | NL, | PL, | PT, | RO, | SE, | SI, |
| | | SK, | TR, | BF, | ВJ, | CF, | CG, | CI, | CM, | GA, | GN, | GQ, | GW, | ML, | MR, | ΝĒ, | SN, |
| | | TD, | TG | | | | | | | | | | | | | | |

PRIORITY APPLN. INFO.:

DK 2003-451 A 20030324 US 2003-459838P P 20030402

OTHER SOURCE(S): MARPAT 141:326195

ED Entered STN: 07 Oct 2004

AB The present invention relates to novel derivs. of human qlucagon-like peptide-2 (GLP-2) peptides which have a protracted profile of action, as well as pharmaceutical compns., uses and methods of treatment.

ICM C07K014-605

A61K038-26; A61P001-00; A61K047-48 ICS

2-6 (Mammalian Hormones)

Section cross-reference(s): 34, 63

Intestine, disease

(Crohn's; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof)

TT Stomach, disease

(atrophic gastritis; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof)

TΤ Intestine, disease

> (atrophy; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof)

IT Intestine, disease

(colitis; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof)

TT Intestine, disease

(enteritis; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof)

IT Stomach, disease

(gastritis; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof)

. IT Intestine, disease

(injury; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof)

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Intestine, disease
        (irritable bowel syndrome; synthesis of protracted GLP-2 derivs.
        attached to an hydrophilic substituent and therapeutic uses thereof)
IT
    Intestine, disease
        (malabsorption; synthesis of protracted GLP-2 derivs. attached to an
        hydrophilic substituent and therapeutic uses thereof)
IT
     Intestine, disease
        (short bowel syndrome; synthesis of protracted GLP-2 derivs. attached
        to an hydrophilic substituent and therapeutic uses thereof)
     768850-00-6DP, polyalkyleneglycol derivs.
                                                 768850-01-7DP,
IT
                                  768850-02-8DP, polyalkyleneglycol derivs.
    polyalkyleneglycol derivs.
     768850-03-9DP, polyalkyleneglycol derivs.
                                                 768850-04-0DP,
    polyalkyleneglycol derivs.
                                  768850-05-1DP, polyalkyleneglycol derivs.
     768850-06-2DP, polyalkyleneglycol derivs.
                                                 768850-07-3DP,
                                  768850-08-4DP, polyalkyleneglycol derivs.
    polyalkyleneglycol derivs.
     768850-09-5DP, polyalkyleneglycol derivs.
                                                 768850-10-8DP,
    polyalkyleneglycol derivs. 768850-11-9DP, polyalkyleneglycol
                                                           768850-13-1DP,
               768850-12-0DP, polyalkyleneglycol derivs.
     polyalkyleneglycol derivs. 768850-14-2DP, polyalkyleneglycol
                                                           768850-17-5DP,
               768850-15-3DP, polyalkyleneglycol derivs.
                                  768850-18-6DP, polyalkyleneglycol derivs.
    polyalkyleneglycol derivs.
     768850-19-7DP, polyalkyleneglycol derivs.
                                                 768850-20-0DP,
                                  768850-21-1DP, polyalkyleneglycol derivs.
     polyalkyleneglycol derivs.
     768850-22-2DP, polyalkyleneglycol derivs. 768850-23-3DP,
                                  768850-24-4DP, polyalkyleneglycol derivs.
     polyalkyleneglycol derivs.
     768850-25-5DP, polyalkyleneglycol derivs. 768850-26-6DP,
                                  768850-27-7DP, polyalkyleneglycol derivs.
     polyalkyleneglycol derivs.
     768850-28-8DP, polyalkyleneglycol derivs.
                                                 768850-29-9DP,
     polyalkyleneglycol derivs.
                                  768850-30-2DP, polyalkyleneglycol derivs.
     768850-31-3DP, polyalkyleneglycol derivs.
                                                 768850-32-4DP,
                                  768850-35-7DP, polyalkyleneglycol derivs.
     polyalkyleneglycol derivs.
     768850-36-8DP, polyalkyleneglycol derivs.
                                                 768850-37-9DP,
                                  768850-38-0DP, polyalkyleneglycol derivs.
     polyalkyleneglycol derivs.
     768850-39-1DP, polyalkyleneglycol derivs.
                                                 768850-40-4DP,
     polyalkyleneglycol derivs. 768850-41-5DP, polyalkyleneglycol
                                                            768850-43-7DP,
               768850-42-6DP, polyalkyleneglycol derivs.
     polyalkyleneglycol derivs. 768850-44-8DP, polyalkyleneglycol
               768850-45-9DP, polyalkyleneglycol derivs. 768850-46-0DP
                                    768850-47-1DP, polyalkyleneglycol derivs.
     , polyalkyleneglycol derivs.
     768850-48-2DP, polyalkyleneglycol derivs. 768850-49-3DP,
                                  768850-50-6DP, polyalkyleneglycol derivs.
     polyalkyleneglycol derivs.
     770731-77-6P 770731-78-7P 770731-79-8P
     RL: BSU (Biological study, unclassified); PAC (Pharmacological
     activity); PRP (Properties); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
     (Uses)
        (amino acid sequence; synthesis of protracted GLP-2 derivs. attached to
        an hydrophilic substituent and therapeutic uses thereof)
     223460-79-5, 1-33-Glucagon-like peptide II (human)
IT
     RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
     (Biological study)
        (amino acid sequence; synthesis of protracted GLP-2 derivs. attached to
        an hydrophilic substituent and therapeutic uses thereof)
                               768850-00-6
                                             768850-01-7
     197922-42-2 197922-46-6
IT
                                                768850-05-1 768850-06-2
                                 768850-04-0
                   768850-03-9
     768850-02-8
                   768850-08-4 768850-09-5
                                             768850-10-8
     768850-07-3
                                 768850-13-1 768850-14-2
                   768850-12-0
     768850-11-9
                               768850-17-5
                                             768850-18-6
     768850-15-3 768850-16-4
                                                768850-22-2 768850-23-3
     768850-19-7
                   768850-20-0
                                 768850-21-1
                   768850-25-5 768850-26-6
                                             768850-27-7
     768850-24-4
     768850-28-8
                   768850-29-9
                                 768850-30-2 768850-31-3
     768850-32-4 768850-33-5 768850-34-6
                                           768850-35-7
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768850-36-8
                  768850-37-9
                                768850-38-0 . 768850-39-1
                                                            768850-40-4
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     768850-41-5
                  768850-42-6
                              768850-47-1 768850-48-2
     768850-45-9 768850-46-0
                  768850-50-6
     RL: PRP (Properties); RCT (Reactant); RACT (Reactant or reagent)
        (amino acid sequence; synthesis of protracted GLP-2 derivs. attached to
        an hydrophilic substituent and therapeutic uses thereof)
L46 ANSWER 5 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN
                        2004:354976 CAPLUS
ACCESSION NUMBER:
                        140:386446
DOCUMENT NUMBER:
                        Synthesis and production of glucagon-like peptide-2
TITLE:
                         (GLP-2) derivatives and, formulations and therapeutic
                        Thim, Lars; Bang, Susanne; Schlein, Morten; Kaarsholm,
INVENTOR (S):
                        Niels Christian; Engelund, Dorthe Kot; Nielsen, Anette
                        Sams; Johansen, Nils Langeland; Madsen, Kjeld; Zundel,
                        Magali; Thygesen, Peter
PATENT ASSIGNEE(S):
                        Novo Nordisk A/S, Den.
                        PCT Int. Appl., 195 pp.
SOURCE:
                        CODEN: PIXXD2
DOCUMENT TYPE:
                        Patent
                        English
LANGUAGE:
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
                        KIND DATE
                                         APPLICATION NO.
                                                                 DATE
    PATENT NO.
                         _ _ _ _
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                                           ______
                                                                  _____
    WO 2004035624
                         A2
                               20040429 WO 2003-DK694
                                                                  20031014
     WO 2004035624
                        A3
                               20040910
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
            CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,
            GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
            LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
            OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
            TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
            KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
            FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
            BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
                                           US 2003-685368
     US 2004122210
                         A1
                               20040624
                                                                  20031014
PRIORITY APPLN. INFO.:
                                           DK 2002-1574
                                                               A 20021014
                                           DK 2002-1778
                                                              A 20021119
                                           DK 2002-1780
                                                              A 20021119
                                           US 2002-420581P
                                                              P 20021023
                                           US 2002-426273P
                                                              P 20021114
                                                              P 20021219
                                           US 2002-434560P
                                                              P 20021219
                                           US 2002-434562P
                        MARPAT 140:386446
OTHER SOURCE(S):
     Entered STN: 30 Apr 2004
     The present invention relates to novel human glucagon-like peptide-2
     (GLP-2) peptides and human glucagon-like peptide-2 derivs. which have a
     protracted profile of action as well as polynucleotide constructs encoding
     such peptides, vectors and host cells comprising and expressing the
     polynucleotide, pharmaceutical compns., uses and methods of treatment.
     ICM C07K014-605
     2-6 (Mammalian Hormones)
     Section cross-reference(s): 16, 34
     Intestine, disease
        (Crohn's; synthesis and production of glucagon-like peptide-2 (GLP-2)
        derivs. and, formulations and therapeutic uses thereof)
    Brain
```

ED

AB

IC

CC

TT

Heart Kidney Liver Lung Muscle Spleen Stomach (GLP-2 receptor expression level in; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof) TΤ Stomach, disease (atrophic gastritis; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof) IT Intestine, disease (colitis; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof) IT Intestine (colon, GLP-2 receptor expression level in; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof) IT Intestine (duodenum, GLP-2 receptor expression level in; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof) IT Intestine, disease (enteritis; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof) Intestine, disease IT (failure; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof) IT Stomach, disease (gastritis; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof) IT (gastrointestinal; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof) IT Intestine (ileum, GLP-2 receptor expression level in; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof) IT Intestine, disease (inflammatory; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof) TT Bone, disease Intestine, disease (injury; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof) IT (jejunum, GLP-2 receptor expression level in; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof) Intestine, disease (malabsorption; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof) ΙT Intestine, disease (mucosa, injury; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof) ΙT Nutrition, animal (parenteral, total, -induced intestinal atrophy; synthesis and production

of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and

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therapeutic uses thereof)
IT
     Intestine, disease
        (short bowel syndrome; synthesis and production of glucagon-like peptide-2
        (GLP-2) derivs. and, formulations and therapeutic uses thereof)
IT
     Intestine, disease
        (ulcerative colitis; synthesis and production of glucagon-like peptide-2
        (GLP-2) derivs. and, formulations and therapeutic uses thereof)
IT
     223460-79-5, 1-33-Glucagon-like peptide II (human)
    RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
     (Biological study)
        (amino acid sequence; synthesis and production of glucagon-like peptide-2
        (GLP-2) derivs. and, formulations and therapeutic uses thereof)
IT
    89750-15-2DP, Glucagon-like peptide II, analogs 682841-20-9P
                                   682841-23-2P
    682841-21-0P
                    682841-22-1P
                                                  682841-24-3P
                                                                  682841-25-4P
    682841-26-5P 682841-27-6P
                                 682841-28-7P
                                                682841-29-8P
                    682841-31-2P 682841-32-3P
    682841-30-1P
                                                682841-33-4P
    682841-34-5P 682841-35-6P
                                 682841-36-7P
                                                682841-37-8P
    682841-38-9P
                    682841-39-0P
                                   682841-40-3P
                                                                  682841-42-5P
                                                  682841-41-4P
                                   682841-45-8P 682841-46-9P
    682841-43-6P
                    682841-44-7P
    682841-47-0P 682841-48-1P
                                 682841-49-2P
                                                682841-50-5P
                    682841-52-7P 682841-53-8P
    682841-51-6P
                                   682841-56-1P
    682841-54-9P
                    682841-55-0P
                                                  682841-57-2P
                                   682841-60-7P 682841-61-8P
    682841-58-3P
                    682841-59-4P
                    682841-63-0P 682841-64-1P
    682841-62-9P
                                                682841-65-2P
                                   682841-68-5P 682841-69-6P
    682841-66-3P
                    682841-67-4P
                    683750-66-5P
                                                                  683750-74-5P
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     683753-00-6P 683753-01-7P 683753-02-8P
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                                              683753-16-4P
     683753-17-5P
                   683753-18-6P
     RL: BMF (Bioindustrial manufacture); PAC (Pharmacological
     activity); SPN (Synthetic preparation); THU (Therapeutic use)
     ; BIOL (Biological study); PREP (Preparation); USES (Uses)
        (synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and,
        formulations and therapeutic uses thereof)
L46 ANSWER 6 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:
                        2002:658156 CAPLUS
DOCUMENT NUMBER:
                        137:180207
TITLE:
                        Preparation of long-lasting glucagon-like peptide 2
                        (GLP-2) analogs and derivatives for the treatment of
                        gastrointestinal diseases and
                        disorders
INVENTOR(S):
                        Bridon, Dominique P.; Boudjellab, Nissab; Leger,
                        Roger; Robitaille, Martin; Thibaudeau, Karen; Carette,
                        Julie
PATENT ASSIGNEE(S):
                        Conjuchem Inc., Can.
SOURCE: PCT Int. Appl., 62 pp.
                                                   CODEN: PIXXD2
DOCUMENT TYPE:
                        Patent
LANGUAGE:
                        English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:
                    KIND
                              DATE
     PATENT NO.
                                        APPLICATION NO.
                                                               DATE
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                              _____
                                          ------
    WO 2002066511
                       A2
                              20020829
                                         WO 2002-CA175
                                                                20020215
    WO 2002066511
                        A3 20030306
            AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
            CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
            GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
            LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
            PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
            UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
            TJ, TM
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
            CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
            BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
                                        CA 2002-2436399
EP 2002-700079
    CA 2436399
                              20020829
                        AA
                                                               20020215
    EP 1360202
                        A2
                              20031112
                                                                20020215
            AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
    JP 2004532819 T2.
                              20041028
                                         JP 2002-566224
                                                                20020215
    US 2004248782
                        A1
                               20041209
                                          US 2002-203808
                                                                20020812
PRIORITY APPLN. INFO.:
                                                            P 20010216
                                          US 2001-269276P
                                                            W 20020215
                                          WO 2002-CA175
                        MARPAT 137:180207
OTHER SOURCE(S):
    Entered STN: 30 Aug 2002
```

This invention relates to glucagon-like peptide 2 (GLP-2) derivs. and

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analogs with gastrointestinal growth promoting activity that have a
reactive entity that makes the peptide capable of bonding to blood
component. In particular, this invention relates to GLP-2 peptide derivs.
having an extended in vivo half-life, for the treatment or prevention of
gastrointestinal disorders or diseases such as inflammatory bowel disease
and other gastrointestinal functions, from any segment of the
qastrointestinal tract, from the esophagus to the anus.
ICM C07K014-605
ICS A61K038-26; A61P001-00
2-6 (Mammalian Hormones)
Section cross-reference(s): 34
long lasting GLP2 deriv analog prepn gastrointestinal
disease treatment
Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
   (blood; preparation of long-lasting glucagon-like peptide 2 (GLP-2) analogs
   and derivs. that bind to blood components for treatment of
 gastrointestinal diseases and disorders)
Drugs
   (gastrointestinal; preparation of long-lasting glucagon-like
   peptide 2 (GLP-2) analogs and derivs. that bind to blood components for
   treatment of gastrointestinal diseases and
   disorders)
Growth factors, animal
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic
preparation); THU (Therapeutic use); BIOL (Biological study); PREP
(Preparation); USES (Uses)
   (gastrointestinal; preparation of long-lasting glucagon-like
   peptide 2 (GLP-2) analogs and derivs. that bind to blood components for
   treatment of gastrointestinal diseases and
   disorders)
Intestine, disease
   (inflammatory; preparation of long-lasting glucagon-like peptide 2
   (GLP-2) analogs and derivs. that bind to blood components for treatment
   of gastrointestinal diseases and disorders
Digestive tract, disease
Drug bioavailability,
Drug design
Protein engineering
   (preparation of long-lasting glucagon-like peptide 2 (GLP-2) analogs and
   derivs. that bind to blood components for treatment of
   gastrointestinal diseases and disorders)
Human
   (preparation of long-lasting human glucagon-like peptide 2 (GLP-2) analogs
   and derivs. that bind to blood components for treatment of
   gastrointestinal diseases and disorders)
Albumins, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
   (serum; preparation of long-lasting glucagon-like peptide 2 (GLP-2) analogs
   and derivs. that bind to blood components for treatment of
   gastrointestinal diseases and disorders)
89750-15-2DP, Glucagon-like peptide 2, derivs. and analogs
99120-49-7DP, Glucagon-like peptide II (human), derivs. and
analogs 451445-88-8P 451445-89-9P 451445-90-2P
451445-91-3P 451445-92-4P 451445-93-5P
                                         451445-94-6P
451445-95-7P
               451445-96-8P 451445-97-9P
451445-98-0P 451445-99-1P 451446-01-8P
                            451446-10-9P
451446-05-2P 451446-09-6P
                                           451446-11-0P
451446-12-1P
              451446-13-2P
                              451446-14-3P
RL: PAC (Pharmacological activity); PKT
(Pharmacokinetics); SPN (Synthetic preparation); THU
```

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of long-lasting glucagon-like peptide 2 (GLP-2) analogs and derivs. that bind to blood components for treatment of gastrointestinal diseases and disorders)

L46 ANSWER 7 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:434877 CAPLUS

DOCUMENT NUMBER: 135:29135

TITLE: Treatment of the adverse effects of chemotherapy with

h[Gly2]-GLP-2

INVENTOR(S): Drucker, Daniel J.; Boushey, Robin P.

PATENT ASSIGNEE(S): 1149336 Ontario Inc., Can. SOURCE: PCT Int. Appl., 36 pp.

CODEN: PIXXD2

DOCUMENT TYPE: LANGUAGE: Patent English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PA | PATENT NO. | | | | KIN | D : | DATE | | | APPL | ICAT | ION 1 | NO. | | D | ATE | |
|---------|--|----------|--------|-----|------------|-----|------|------|-----|------|------|-------|------|-----|------|------|-----|
| WO | 2001 | 0417 | 79 | | A2 | - | 2001 | 0614 | | WO 2 | 000- | IB20 | 03 | | 2 | 0001 | 208 |
| WO | 2001 | 0417 | 79 | | A 3 | | 2002 | 0110 | | | | | | | | | |
| | W: | ΑE, | AG, | AL, | AM, | ΑT, | AU, | ΑZ, | BA, | BB, | BG, | BR, | BY, | BZ, | CA, | CH, | CN, |
| | | CR, | CU, | CZ, | DE, | DK, | DM, | DZ, | EĖ, | ES, | FI, | GB, | GD, | GE, | GH, | GM, | HR, |
| | | HU, | ID, | IL, | IN, | IS, | JP, | KE, | KG, | ΚP, | KR, | KZ, | LC, | LK, | LR, | LS, | LT, |
| | | LU, | LV, | MA, | MD, | MG, | MK, | MN, | MW, | MX, | MZ, | NO, | NZ, | PL, | PT, | RO, | RU, |
| | | SD, | SE, | SG, | SI, | SK, | SL, | ТJ, | TM, | TR, | TT, | TZ, | UA, | UG, | US, | UZ, | VN, |
| | | YU, | ZA, | ZW, | AM, | AZ, | BY, | KG, | KZ, | MD, | RU, | ТJ, | TM | | | | |
| | RW: | GH, | GM, | KE, | LS, | MW, | MZ, | SD, | SL, | SZ, | TZ, | UG, | ZW, | AT, | BE, | CH, | CY, |
| - | | | | | | | | | | | LU, | | | | | | |
| | | ВJ, | CF, | CG, | CI, | CM, | GA, | GN, | GW, | ML, | MR, | NE, | SN, | TD, | TG | | |
| US | 2003 | 0404 | 78 | | A1 | | 2003 | 0227 | | US 2 | 002- | 1486 | 82 | | 2 | 0020 | 722 |
| PRIORIT | US 2003040478 RIORITY APPLN. INFO.: | | | | | | | | | US 1 | 999- | 1696 | 54 P | | A2 1 | 9991 | 208 |
| | RIORIII AII LA. INIO | | | | | | | | | US 2 | -000 | 1807 | 79P | | A2 2 | 0000 | 207 |
| | | | | | | | | | | US 2 | -000 | 2239 | 75P | | A2 2 | 0000 | 809 |
| | | | | | | | | | | US 2 | 000- | 2427. | 54P | | A2 2 | 0001 | 025 |
| | | | | | | | | | | WO 2 | 000- | IB20 | 03 | 1 | W 2 | 0001 | 208 |

ED Entered STN: 15 Jun 2001

AΒ This invention provides a treatment regimen that is effective in inhibiting chemotherapy-induced apoptosis and promoting cell survival. The invention also relates to a treatment regimen that confers resistance to caspase activation, thereby inhibiting caspase-mediated, proteolytic cleavage of functional cellular enzymes. Specifically, subjects undergoing chemotherapy are first exposed to a pretreatment regimen. Under this regimen, a GLP-2 receptor activator, such as h[Gly2]-GLP-2, is administered each day for a predetd. beneficial period, e.g., three consecutive days. Approx. about 1 wk following pretreatment, the subjects are exposed to an appropriate chemotherapy treatment regimen. Pretreatment with a GLP-2 receptor activator followed by administration of chemotherapeutic agents improves cell survival, reduces bacteremia, attenuates epithelial injury, and inhibits cellular apoptosis. Moreover, it does not impair the effectiveness of chemotherapy nor result in weight loss. The anti-apoptotic effects of GLP-2 may be useful in the reduction of cytotoxicity and bacterial infection induced by chemotherapeutic agents.

IC ICM A61K038-00

CC 1-6 (Pharmacology)

Section cross-reference(s): 2

IT Intestine

(colon, crypt cell, loss; treatment with h[Gly2]-GLP-2 to attenuate cancer chemotherapy-induced adverse apoptosis and to promote cell

survival)

IT Intestine

(crypt, loss; treatment with h[Gly2]-GLP-2 to attenuate cancer chemotherapy-induced adverse apoptosis and to promote cell survival)

IT Intestine

(epithelium, integrity; treatment with h[Gly2]-GLP-2 to attenuate cancer chemotherapy-induced adverse apoptosis and to promote cell survival)

IT Intestine

(jejunum, crypt, loss; treatment with h[Gly2]-GLP-2 to attenuate cancer chemotherapy-induced adverse apoptosis and to promote cell survival)

IT 197922-42-2

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(treatment with h[Gly2]-GLP-2 to attenuate cancer chemotherapy-induced adverse apoptosis and to promote cell survival)

L46 ANSWER 8 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

2001:91506 CAPLUS

DOCUMENT NUMBER:

134:168296

TITLE:

INVENTOR(S):

Intestinotrophic glucagon-like peptide-2 analogs
Drucker, Daniel J.; Crivici, Anna E.; Sumner-Smith,

Martin

PATENT ASSIGNEE(S):

NPS Allelix Corp., Can.

SOURCE:

U.S., 16 pp., Cont.-in-part of U.S. Ser. No. 631,273,

abandoned.

CODEN: USXXAM

DOCUMENT TYPE:

Patent English

LANGUAGE:

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------------|-----------|---|---------------|
| | | | *************************************** | 10070400 |
| US 6184201 | B1 | 20010206 | US 1997-835538 | 19970408 |
| US 5990077 | Α | 19991123 | US 1995-422540 | 19950414 |
| US 5789379 | Α | 19980804 | US 1996-669791 | 19960628 |
| US 5834428 | Α | 19981110 | US 1996-669790 | 19960628 |
| US 2001021767 | A 1 | 20010913 | US 2001-764070 | 20010119 |
| EP 1231219 | A1 | 20020814 | EP 2001-129072 | 20011207 |
| R: AT, BE, CH, | DE, DK | , ES, FR, | GB, GR, IT, LI, LU, NL | , SE, MC, PT, |
| IE, FI | | | | |
| US 2003162703 | A1 | 20030828 | US 2002-293941 | 20021114 |
| US 2003158101 | A1 | 20030821 | US 2002-42746 | 20021120 |
| PRIORITY APPLN. INFO.: | | | US 1995-422540 | A2 19950414 |
| | • | | US 1996-631273 | B2 19960412 |
| | | | US 1996-632533 | B2 19960412 |
| | | | US 1997-835538 | A3 19970408 |
| | | | US 2001-764070 | A1 20010119 |
| | | | EP 1997-916280 | A3 20011207 |

OTHER SOURCE(S): MARPAT 134:168296

ED Entered STN: 07 Feb 2001

AB Analogs of glucagon-like peptide 2, a product of glucagon gene expression, have been identified as intestinal tissue growth factors. Their formulation as pharmaceuticals and therapeutic use in treating disorders of the small bowel are described.

IC ICM A61K038-26

ICS A61K038-17; C07K014-605

NCL 514012000

CC 63-3 (Pharmaceuticals)

Section cross-reference(s): 2

```
IT
     Intestine, disease
        (Crohn's; intestinotrophic glucagon-like peptide-2 analogs)
IT
        (disease; intestinotrophic glucagon-like peptide-2 analogs)
IT
     Intestine, disease
        (enteritis; intestinotrophic glucagon-like peptide-2 analogs)
IT
     Intestine, disease
        (inflammatory; intestinotrophic glucagon-like peptide-2
        analogs)
IT
     Intestine, disease
        (malabsorption; intestinotrophic glucagon-like peptide-2 analogs)
IT
     Intestine, disease
        (short bowel syndrome; intestinotrophic glucagon-like peptide-2
        analogs)
IT
     Intestine, disease
        (small; intestinotrophic glucagon-like peptide-2 analogs)
TT
     223460-79-5, 1-33-Glucagon-like peptide II (human)
     325150-33-2
     RL: PRP (Properties)
        (unclaimed protein sequence; intestinotrophic qlucagon-like peptide-2
        analogs)
REFERENCE COUNT:
                         29
                               THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
L46 ANSWER 9 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:
                         2001:125542 CAPLUS
DOCUMENT NUMBER:
                         134:173276
TITLE:
                         Glucagon-like peptide (GLP)-2 reduces
                         chemotherapy-associated mortality and enhances cell
                         survival in cells expressing a transfected GLP-2
                         receptor
AUTHOR (S):
                         Boushey, Robin P.; Yusta, Bernardo; Drucker, Daniel J.
CORPORATE SOURCE:
                         Banting and Best Diabetes Centre, University of
                         Toronto, Toronto, ON, M5G 2C4, Can.
SOURCE:
                         Cancer Research (2001), 61(2), 687-693
                         CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER:
                         American Association for Cancer Research
DOCUMENT TYPE:
                         Journal
LANGUAGE:
                         English
ED
     Entered STN: 21 Feb 2001
AΒ
     Chemotherapeutic agents produce cytotoxicity via induction of apoptosis
     and cell cycle arrest. Rapidly proliferating cells in the bone marrow and
     intestinal crypts are highly susceptible to chemotherapy, and damage to
     these cellular compartments may preclude maximally effective chemotherapy
     administration. Glucagon-like peptide (GLP)-2 is an enteroendocrine-
     derived regulatory peptide that inhibits crypt cell apoptosis after
     administration of agents that damage the intestinal epithelium. We report
     here that a human degradation-resistant GLP-2 analog, h[Gly2]-GLP-2
     significantly improves survival, reduces bacteremia, attenuates epithelial
     injury, and inhibits crypt apoptosis in the murine gastrointestinal tract
     after administration of topoisomerase I inhibitor irinotecan hydrochloride
     or the antimetabolite 5-fluorouracil. The analog h[Gly2]-GLP-2
     significantly improved survival and reduced weight loss but did not impair
     chemotherapy effectiveness in tumor-bearing mice treated with cyclical
     irinotecan. Furthermore, h[Gly2]-GLP-2 reduced chemotherapy-induced
     apoptosis, decreased activation of caspase-8 and -3, and inhibited
     poly(ADP-ribose) polymerase cleavage in heterologous cells transfected
    with the GLP-2 receptor. These observations demonstrate that the
     antiapoptotic effects of GLP-2 on intestinal crypt cells may be useful for
     the attenuation of chemotherapy-induced intestinal mucositis.
     2-6 (Mammalian Hormones)
     Section cross-reference(s): 1
```

IT Intestine (crypt; GLP-2 analog reduces chemotherapy-associated mortality and enhances cell survival in cells expressing transfected GLP-2 receptor) 197922-42-2, Glucagon-like peptide II [2-glycine] (human) IT RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (GLP-2 analog reduces chemotherapy-associated mortality and enhances cell survival in cells expressing transfected GLP-2 receptor) REFERENCE COUNT: THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT L46 ANSWER 10 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN 2001:369259 CAPLUS ACCESSION NUMBER: DOCUMENT NUMBER: 135:235705 ALX-0600 (NPS Allelix Corp) TITLE: Sigalet, David L. AUTHOR (S): Department of Surgery, University of Calgary, Calgary, CORPORATE SOURCE: AB, T2N 4N1, Can. SOURCE: Current Opinion in Investigational Drugs (PharmaPress Ltd.) (2001), 2(4), 505-509 CODEN: COIDAZ PUBLISHER: PharmaPress Ltd. DOCUMENT TYPE: Journal; General Review English LANGUAGE: Entered STN: 23 May 2001 A review with many refs. NPS Allelix (formerly Allelix Biopharmaceuticals) is developing the glucagon-like peptide 2 (GLP-2) analog ALX-0600 for the potential treatment of gastrointestinal diseases, including short bowel disease. GLP stimulates the growth of the lining of the small intestine, thus increasing the absorptive area of the intestine. ALX-0600 also has potential for mucositis associated with cancer chemotherapy and inflammatory bowel disease. During the third quarter of 1999, a pilot phase II trial began for short bowel syndrome (SBS). ALX-0600 began pivotal phase II trials in 2000 following the completion of the pilot trial which was designed to measure the safety, tolerability, and any other drug-related improvements in nutrient absorption and phys. changes in the gut of a small number of patients with SBS. Allelix hopes to bring this drug to the market by 2001. Allelix filed an application to the FDA for Orphan Drug designation in the third quarter of 1999; in August, the designation was approved. As of Nov. 1998, Allelix was in discussions with a potential marketing partner for worldwide development and marketing. In August 1998, the USPTO issued a notice of allowance to Allelix for its basic patent containing claims covering the composition and medical uses of ALX-0600 and related GI drug candidate compds. 1-0 (Pharmacology) ST review ALX0600 glucagonlike peptide gastrointestinal disease IT Digestive tract (disease; glucagon-like peptide 2 (GLP-2) analog ALX-0600 for potential treatment of gastrointestinal diseases, including short bowel disease in humans) 89750-15-2, Glucagon-like peptide 2 IT RL: BSU (Biological study, unclassified); BIOL (Biological study) (analog; glucagon-like peptide 2 (GLP-2) analog ALX-0600 for potential treatment of gastrointestinal diseases, including short bowel disease in humans) IT 197922-42-2, ALX-0600 RL; ADV (Adverse effect, including toxicity); BAC (Biological activity or

effector, except adverse); BSU (Biological study, unclassified); THU

(qlucagon-like peptide 2 (GLP-2) analog ALX-0600 for potential

(Therapeutic use); BIOL (Biological study); USES (Uses)

treatment of gastrointestinal diseases, including short bowel disease in humans)

REFERENCE COUNT:

42 THERE

THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 11 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

2000:910724 CAPLUS

DOCUMENT NUMBER:

134:66461

TITLE:

GLP-2 stimulates intestinal growth in premature

AUTHOR(S):

TPN-fed pigs by suppressing proteolysis and apoptosis Burrin, D. G.; Stoll, B.; Jiang, R.; Petersen, Y.; Elnif, J.; Buddington, R. K.; Schmidt, M.; Holst, J.

J.; Hartmann, B.; Sangild, P. T.

CORPORATE SOURCE:

Agricultural Research Service, Children's Nutrition Research Center, Department of Pediatrics, Baylor College of Medicine, United States Department of

Agriculture, Houston, TX, 77030, USA

SOURCE:

American Journal of Physiology (2000), 279(6, Pt. 1),

G1249-G1256

CODEN: AJPHAP; ISSN: 0002-9513 American Physiological Society

PUBLISHER:
DOCUMENT TYPE:
LANGUAGE:

Journal English

ED Entered STN: 29 Dec 2000

AΒ The authors wished to determine whether exogenous glucagon-like peptide (GLP)-2 infusion stimulates intestinal growth in parenterally fed immature pigs. Piglets (106-108 days gestation) were given parenteral nutrient infusion (TPN), TPN + human GLP-2 (25 nmol·kg-1·day-1), or sow's milk enterally (ENT) for 6 days. Intestinal protein synthesis was then measured in vivo after a bolus dose of [1-13C]phenylalanine, and degradation was calculated from the difference between protein accretion and synthesis. Crypt cell proliferation and apoptosis were measured in situ by 5-bromodeoxyuridine (BrdU) and terminal dUTP nick-end labeling (TUNEL), Intestinal protein and DNA accretion rates and villus heights were similar in GLP-2 and ENT pigs, and both were higher (P < 0.05) than in TPN pigs. GLP-2 decreased fractional protein degradation rate, whereas ENT increased fractional protein synthesis rate compared with TPN pigs. Percentage of TUNEL-pos. cells in GLP-2 and ENT groups was 48 and 64% lower, resp., than in TPN group (P < 0.05). However, ENT, but not GLP-2, increased percentage of BrdU-pos. crypt cells above that in TPN piglets. The authors conclude that GLP-2 increases intestinal growth in premature, TPN-fed pigs by decreasing proteolysis and apoptosis, whereas enteral nutrition acts via increased protein synthesis and cell proliferation and decreased apoptosis.

CC 2-6 (Mammalian Hormones)

Section cross-reference(s): 18

IT Nutrition, animal

(enteral; enteral nutrition stimulates intestinal growth via increased protein synthesis and cell proliferation and decreased apoptosis in premature pigs)

IT Nutrition, animal

(parenteral, total; GLP-2 stimulates intestinal growth in premature TPN-fed pigs by suppressing proteolysis and apoptosis)

IT 223460-79-5, Human glucagon like peptide-2

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(GLP-2 stimulates intestinal growth in premature TPN-fed pigs by suppressing proteolysis and apoptosis)

REFERENCE COUNT:

31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

. L46 ANSWER 12 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN

Page 21

2000:270743 CAPLUS ACCESSION NUMBER:

133:41523 DOCUMENT NUMBER:

TITLE: Circulating levels of glucagon-like peptide-2 in human

subjects with inflammatory bowel disease

Xiao, Qiang; Boushey, Robin P.; Cino, Maria; Drucker, AUTHOR (S):

Daniel J.; Brubaker, Patricia L.

CORPORATE SOURCE:

Department of Physiology, Mount Sinai Hospital and the Toronto General Hospital, Toronto, ON, M5G 2C4, Can.

SOURCE: American Journal of Physiology (2000), 278(4, Pt. 2),

R1057-R1063

CODEN: AJPHAP; ISSN: 0002-9513

American Physiological Society PUBLISHER:

Journal DOCUMENT TYPE: English LANGUAGE: Entered STN: 26 Apr 2000

Glucagon-like peptide-2 (GLP-2) is a recently characterized intestine-derived peptide that exerts trophic activity in the small and large intestine. Whether circulating levels of GLP-2 are perturbed in the setting of human inflammatory bowel disease (IBD) remains unknown. circulating levels of bioactive GLP-2-(1-33) compared with its degradation product GLP-2-(3-33) were assessed using a combination of RIA and HPLC in normal and immunocompromised control human subjects and patients hospitalized for IBD. The activity of the enzyme dipeptidyl peptidase IV (DP IV), a key determinant of GLP-2-(1-33) degradation was also assessed in the plasma of normal controls and subjects with IBD. The circulating levels of bioactive GLP-2-(1-33) were increased in patients with either ulcerative colitis (UC) or Crohn's disease (CD; to 229 and 317%, of normal, resp.). Furthermore, the proportion of total immunoreactivity represented by intact GLP-2-(1-33), compared with GLP-2-(3-33), was increased from 43% in normal healthy controls to 61% and 59% in patients with UC and CD, resp. The relative activity of plasma DP IV was reduced in subjects with IBD compared with normal subjects (1.4 vs. 5.0 mU/mL, resp.). Thus, patients with active IBD may undergo an adaptive response

14-7 (Mammalian Pathological Biochemistry) CC Section cross-reference(s): 2

IT Intestine, disease

epithelium in vivo.

(Crohn's; circulating levels of glucagon-like peptide-2 in human subjects with inflammatory bowel disease)

to intestinal injury by increasing the circulating levels of bioactive GLP-2-(1-33), facilitating enhanced repair of the intestinal mucosal

IT Intestine, disease

(inflammatory; circulating levels of glucagon-like peptide-2 in human subjects with inflammatory bowel disease)

IT Intestine, disease

(injury; circulating levels of glucagon-like peptide-2 in human subjects with inflammatory bowel disease)

IT Intestine, disease

> (ulcerative colitis; circulating levels of glucagon-like peptide-2 in human subjects with inflammatory bowel disease)

89750-15-2, Glucagon-like peptide II 223460-79-5, IT

1-33-Glucagon-like peptide II (human) 275801-62-2, 3-33-Glucagon-like peptide II (human)

RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)

(circulating levels of glucagon-like peptide-2 in human subjects with inflammatory bowel disease)

REFERENCE COUNT: THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 13 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN 2000:545056 CAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER:

133:261763

TITLE:

Glucagon-like peptide-2 enhances intestinal epithelial

barrier function of both transcellular and

paracellular pathways in the mouse

AUTHOR(S):

Benjamin, M. A.; McKay, D. M.; Yang, P-C.; Cameron,

H.; Perdue, M. H.

CORPORATE SOURCE:

Intestinal Disease Research Program, McMaster

University, Hamilton, ON, Can.

Gut (2000), 47(1), 112-119

CODEN: GUTTAK; ISSN: 0017-5749

PUBLISHER:

SOURCE:

BMJ Publishing Group

DOCUMENT TYPE:

Journal English

LANGUAGE:

Entered STN: 09 Aug 2000 ED

AB Glucagon-like peptide-2 (GLP-2) is a recently identified potent intestinotrophic factor. We have evaluated the effect of GLP-2 treatment on intestinal epithelial barrier function in mice. CD-1 mice were injected s.c. with GLP-2 or a protease resistant analog, h[Gly2]GLP-2, twice daily for up to 10 days. Saline injected mice served as controls. Jejunal segments were mounted in Ussing chambers. Tissue conductance was measured and unidirectional fluxes were determined for (i) Na+ and the small inert probe Cr-EDTA (both transported via the paracellular pathway) and (ii) the macromol. horseradish peroxidase (HRP, transported via the transcellular pathway). Mice treated with GLP-2 or h[Gly2]GLP-2 for 10 days demonstrated significantly reduced intestinal conductance and fluxes of Na+, Cr-EDTA, and HRP. Electron microscopy confirmed that GLP-2 reduced endocytic uptake of HRP into enterocytes. Functional changes (evident by four hours) preceded morphol. changes (evident by 48 h). GLP-2 enhances intestinal epithelial barrier function by affecting both paracellular and transcellular pathways and thus may be of therapeutic value in a number of gastrointestinal conditions.

CC 2-6 (Mammalian Hormones)

ITIntestine

> (epithelium; glucagon-like peptide-2 enhances intestinal epithelial barrier function of both transcellular and paracellular pathways in mice)

Intestine IT

> (jejunum; glucagon-like peptide-2 enhances intestinal epithelial barrier function of both transcellular and paracellular pathways in

89750-15-2, Glucagon-like peptide-2 197922-42-2, Glucagon-like IT peptide II [2-glycine] (human)

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(glucagon-like peptide-2 enhances intestinal epithelial barrier function of both transcellular and paracellular pathways in mice)

REFERENCE COUNT:

THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 14 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

2000:322422 CAPLUS 133:145191

DOCUMENT NUMBER: TITLE:

Glucagon-like Peptide 2: A New Treatment for

Chemotherapy-Induced Enteritis

AUTHOR (S):

Tavakkolizadeh, A.; Shen, R.; Abraham, P.; Kormi, N.; Seifert, P.; Edelman, E. R.; Jacobs, D. O.; Zinner, M.

J.; Ashley, S. W.; Whang, E. E.

CORPORATE SOURCE:

Department of Surgery, Brigham and Women's Hospital,

Boston, MA, 02115, USA

SOURCE:

Journal of Surgical Research (2000), 91(1), 77-82

CODEN: JSGRA2; ISSN: 0022-4804

Harle 10/042746 Page 23

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal LANGUAGE: English ED Entered STN: 18 May 2000

AΒ Background. Glucagon-like peptide 2 (GLP-2) is a recently identified intestinal epithelium-specific growth factor that has been shown to reduce the severity of inflammatory disorders of the intestine in rodent models. The authors hypothesized that GLP-2 administration would be beneficial in chemotherapy-induced enteritis either by preventing injury or by promoting recovery. Material and methods. Rats received no drug (control), chemotherapy alone [5-fluorouracil (5-FU), 190 mg/kg, i.p.] (Chemo), 5-FU followed by 3 days of GLP-2 analog (ALX-0600, 0.1 µg, s.c. twice daily) (CH-G), or GLP-2 analog for 6 days prior to 5-FU and for 3 days afterward (G-CH-G). Animals were pair fed. Rats received 5-bromo-2-deoxyuridine (Br-dU, 50 mg/kg, 2.5 h prior to sacrifice on Day 3 postchemotherapy) for immunohistochem. assessment of cellular proliferation. Results. Chemotherapy induced significant redns. in body weight, villus height, and crypt depth compared with controls. Intestinal wet weight, villus height, and crypt depth were significantly higher for the CH-G group compared with the Chemo group. The CH-G group also showed a significant improvement in villus height compared with the G-CH-G group. Crypt depth, but not jejunal wet weight or villus height, was significantly improved in the G-CH-G group compared with the Chemo group. The percentage of Br-dU-labeled cells in the intestinal crypts did not differ among the groups. These results suggest, for the first time, that GLP-2 Conclusions. treatment initiated after chemotherapy administration enhances intestinal recovery. In contrast, GLP-2 treatment initiated prior to chemotherapy administration to prevent injury has less beneficial effect. administration may be beneficial to patients suffering from chemotherapy-induced enteritis. (c) 2000 Academic Press.

CC 2-6 (Mammalian Hormones)

IT Intestine

(crypt; glucagon-like peptide 2 in treatment of chemotherapy-induced enteritis in rats)

IT Intestine, disease

(enteritis; glucagon-like peptide 2 in treatment of chemotherapy-induced enteritis in rats)

IT Intestine

(villus; glucagon-like peptide 2 in treatment of chemotherapy-induced enteritis in rats)

IT 197922-42-2, ALX 0600

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

(glucagon-like peptide 2 in treatment of chemotherapy-induced enteritis in rats)

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 15 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:736497 CAPLUS

DOCUMENT NUMBER: 131:318292

TITLE: Glucagon-related peptides and their use for the

prevention or treatment of disorders involving the

large intestine Drucker, Daniel J.

INVENTOR(S): Drucker, Daniel J.
PATENT ASSIGNEE(S): 1149336 Ontario Inc., Can.

SOURCE: PCT Int. Appl., 40 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

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PATENT NO.
                         KIND
                                DATE
                                           APPLICATION NO.
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     WO 9958144
                                19991118
                                            WO 1998-CA477
                         A1
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         W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
             DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG,
             KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,
             NO, NZ, PL, PT, RO, RU
         RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
             FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CI, CM,
             GA, GN, ML, MR, NE, SN, TD, TG
     AU 9874215
                          Α1
                                19991129
                                            AU 1998-74215
                                                                   19980511
PRIORITY APPLN. INFO.:
                                            WO 1998-CA477
                                                                A 19980511
     Entered STN: 19 Nov 1999
AB
     The invention relates to glucagon-related peptides and their use for the
     prevention or treatment of disorders involving the large intestine. In
     particular, it has now been demonstrated that GLP-2 and peptidic agonists
     of GLP-2 can cause proliferation of the tissue of large intestine. Thus,
     the invention provides methods of proliferating the large intestine in a
     subject in need thereof. Further, the methods of the invention are useful
     to treat or prevent inflammatory conditions of the large intestine,
     including inflammatory bowel diseases.
     A61K038-26; G01N038-26
IC
CC
     2-6 (Mammalian Hormones)
IT
     Intestine, disease
        (Crohn's; glucagon-related peptides and use for prevention or treatment
        of disorders involving the large intestine)
IT
     Gastrointestinal hormone receptors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (GLP-2 receptors, agonists; glucagon-related peptides and use for
        prevention or treatment of disorders involving the large
        intestine)
IT
     Intestine, disease
        (colitis, infections, ischemic, drug-induce colitis, or chemical-induced
        colitis; glucagon-related peptides and use for prevention or treatment
        of disorders involving the large intestine)
IT
     Intestine, disease
        (colitis; glucagon-related peptides and use for prevention or treatment
        of disorders involving the large intestine)
IT
     Intestine, disease
        (diverticulitis; glucagon-related peptides and use for prevention or
        treatment of disorders involving the large intestine)
IT
     Intestine, disease
        (inflammatory; glucagon-related peptides and use for
        prevention or treatment of disorders involving the large
        intestine)
IT
     Intestine
        (large; glucagon-related peptides and use for enhancing functioning of
        the large intestine by causing proliferation)
IT
     Intestine
        (resection; glucagon-related peptides and use for prevention or
        treatment of disorders involving the large intestine)
IT
     Intestine, disease
        (ulcerative colitis; glucagon-related peptides and use for prevention
        or treatment of disorders involving the large intestine)
IT
     89750-15-2, Glucagon like peptide-2 195262-56-7
     195262-56-7D, analogs 197664-29-2 197922-42-2
     197922-60-4 197923-49-2 223460-79-5,
     1-33-Glucagon-like peptide II (human) 223460-79-5D,
     1-33-Glucagon-like peptide II (human), analogs
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
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study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(glucagon-related peptides and use for prevention or treatment of disorders involving the large intestine)

REFERENCE COUNT:

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 16 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN

4

ACCESSION NUMBER:

1999:565944 CAPLUS

DOCUMENT NUMBER:

131:189728

TITLE:

GLP-2 derivatives with helix-content exceeding 25 %, forming partially structured micellar-like aggregates

INVENTOR (S):

Knudsen, Liselotte Bjerre; Huusfeldt, Per Olaf; Nielsen, Per Franklin; Kaarsholm, Niels C.; Olsen,

ADDITCATION NO

חמידים

Helle Birk; Thim, Lars; Bjorn, Soren Erik Novo Nordisk A/s, Den.

PATENT ASSIGNEE(S):

PCT Int. Appl., 24 pp.

SOURCE:

CODEN: PIXXD2

DATE

DOCUMENT TYPE:

Patent

LANGUAGE:

English

KIND

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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| PA | PATENT NO. | | | | | ט | DATE | | AP | | | | NO. | | D. | ATE | | |
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| WO | 9943 | 361 | | | A1 | <u> </u> | 1999 | 0902 | WO | | | DK80 | | | 1 | 9990: | 225 | |
| | W: | AL, | AM, | ΑT, | AU, | ΑZ, | BA, | BB, | BG, B | R, | BY, | CA, | CH, | CN, | CU, | CZ, | DE, | |
| | | DK, | EE, | ES, | FI, | GB, | GD, | GE, | GH, G | Μ, | HR, | HU, | ID, | IL, | IN, | IS, | JP, | |
| | | KE, | KG, | ΚP, | KR, | ΚZ, | LC, | LK, | LR, L | s, | LT, | LU, | LV, | MD, | MG, | MK, | MN, | |
| | | MW, | MX, | NO, | NZ, | PL, | PT, | RO, | RU, S | D, | SE, | SG, | SI, | SK, | SL, | ТJ, | TM, | |
| | | TR, | TT, | UA, | UG, | UΖ, | VN, | ΥU, | ZW, A | Μ, | ΑZ, | BY, | KG, | ΚZ, | MD, | RU, | ΤJ, | TM |
| | RW: | GH, | GM, | KE, | LS, | MW, | SD, | SL, | SZ, U | ΙĠ, | ZW, | ΑT, | BE, | CH, | CY, | DE, | DK, | |
| | | • | • | | • | • | • | | LU, M | | | | SE, | BF, | ВJ, | CF, | CG, | |
| | | CI, | CM, | GΑ, | GN, | GW, | ML, | MR, | NE, S | N, | TD, | TG | | | | | | |
| AU | 9927 | 128 | | | A1 | | | | AU | | | | | | 1 | 9990: | 225 | |
| EP | 1060 | | | | A2 | | | | EP | | | | | | | 9990: | | |
| | R: | AT, | BE, | • | • | | - | - | GB, G | - | - | | | | | | | FI |
| | 2002 | | | | T2 | | | | JP | | | | | | | | | |
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| | | | | | A1 | | 2004 | 0701 | US | | | | | | | | | |
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| | | | | | | | | | | | | | 87 | | | 9990: | | |
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| | | | | | | | | - | US | 20 | 001- | 9085 | 34 | | A1 2 | 0010 | 718 | |

OTHER SOURCE(S): MARPAT 131:189728

ED Entered STN: 08 Sep 1999

AB The present invention relates to a pharmaceutical composition comprising a GLP-2 derivative of improved solubility and/or stability, and to a method for improving the solubility and/or stability of GLP-2 or a fragment or an analog thereof. Lys30 [Nε-[γ-glutamyl (Nα-tetradecanoyl)]] hGLP-

2 was prepared from hGLP-2-OH, EDPA, NMP and Myr-Glu(ONSu)-OBu-tert.

IC ICM A61K058-26

ICS C07K014~605

CC 63-6 (Pharmaceuticals)

IT Intestine, disease

(Crohn's; GLP-2 derivs. with helix-content exceeding 25% forming

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partially structured micellar-like aggregates)
IT
     Aggregates
     Buffers
       Intestine, disease
       Intestine, neoplasm
     Micelles
     Preservatives
     Surfactants
     Ulcer
        (GLP-2 derivs. with helix-content exceeding 25% forming partially
        structured micellar-like aggregates)
IT
     Intestine, disease
        (enteritis; GLP-2 derivs. with helix-content exceeding 25% forming
        partially structured micellar-like aggregates)
IT
     Intestine, disease
        (ileitis; GLP-2 derivs. with helix-content exceeding 25% forming
        partially structured micellar-like aggregates)
IT
     Intestine, disease
        (inflammatory; GLP-2 derivs. with helix-content exceeding 25%
        forming partially structured micellar-like aggregates)
     99120-49-7, Glucagon-like peptide II (human)
IT
                                                    204521-61-9
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (GLP-2 derivs. with helix-content exceeding 25% forming partially
        structured micellar-like aggregates)
TT
     240483-73-2P
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL
     (Biological study); PREP (Preparation); USES (Uses)
        (GLP-2 derivs. with helix-content exceeding 25% forming partially
        structured micellar-like aggregates)
     99120-49-7D, Glucagon-like peptide II (human), derivs.
IT
    204401-91-2-204401-92-3 204401-93-4
     240484-09-7 240485-39-6 240485-42-1
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (GLP-2 derivs. with helix-content exceeding 25% forming partially
        structured micellar-like aggregates)
REFERENCE COUNT:
                               THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS
                         6
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
L46 ANSWER 17 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:
                         1999:767688 CAPLUS
DOCUMENT NUMBER:
                         132:59448
TITLE:
                         Glucagon-like peptide 2 decreases mortality and
                         reduces the severity of indomethacin-induced murine
                         enteritis
                         Boushey, Robin P.; Yusta, Bernardo; Drucker, Daniel J.
AUTHOR(S):
CORPORATE SOURCE:
                         Department of Medicine, Banting and Best Diabetes
                         Centre, The Toronto General Hospital, University of
                         Toronto, Toronto, ON, M5G2C4, Can.
SOURCE:
                         American Journal of Physiology (1999), 277(5, Pt. 1),
                         E937-E947
                         CODEN: AJPHAP; ISSN: 0002-9513
PUBLISHER:
                         American Physiological Society
DOCUMENT TYPE:
                         Journal
LANGUAGE:
                         English
     Entered STN: 06 Dec 1999
     Glucagon-like peptides (GLPs) are secreted from enteroendocrine cells in
     the gastrointestinal tract. GLP-1 actions regulate blood glucose, whereas
    GLP-2 exerts trophic effects on intestinal mucosal epithelium. Although
     GLP-1 actions are preserved in diseases such as diabetes, GLP-2 action has
     not been extensively studied in the setting of intestinal disease. We
    have now evaluated the biol. effects of a human GLP-2 analog in the
     setting of exptl. murine nonsteroidal antiinflammatory drug-induced
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Harle 10/042746

enteritis. Human (h) [Gly2]GLP-2 significantly improved survival whether administered before, concomitant with, or after indomethacin. The h[Gly2]GLP-2-treated mice exhibited reduced histol. evidence of disease activity, fewer intestinal ulcerations, and decreased myeloperoxidase activity in the small bowel (vs. saline-treated controls). The h[Gly2]GLP-2 significantly reduced cytokine induction, bacteremia, and the percentage of pos. splenic and hepatic bacterial cultures. The h[Gly2]GLP-2 enhanced epithelial proliferation (for increased crypt cell proliferation in h[Gly2]GLP-2- vs. saline-treated mice after indomethacin) and reduced apoptosis in the crypt compartment. These observations demonstrate that a human GLP-2 analog exerts multiple complementary actions that serve to preserve the integrity of the mucosal epithelium in exptl. gastrointestinal injury in vivo.

CC 2-6 (Mammalian Hormones)

T Intestine, disease

(enteritis; glucagon-like peptide 2 decreases mortality and reduces severity of indomethacin-induced murine enteritis)

IT Intestine

CORPORATE SOURCE:

PUBLISHER:

(small; glucagon-like peptide 2 decreases mortality and reduces severity of indomethacin-induced murine enteritis)

IT 197922-42-2, Glucagon-like peptide II [2-glycine] (human)

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(glucagon-like peptide 2 decreases mortality and reduces severity of indomethacin-induced murine enteritis)

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 18 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:73299 CAPLUS

DOCUMENT NUMBER: 130:218560

TITLE: Human [Gly2]GLP-2 reduces the severity of colonic injury in a murine model of experimental colitis AUTHOR(S): Drucker, Daniel J.; Yusta, Bernardo; Boushey, Robin

P.; Deforest, Lorraine; Brubaker, Patricia L. Department of Medicine, Banting and Best Diabetes

Centre, Toronto Hospital, ON, Can.

SOURCE: American Journal of Physiology (1999), 276(1, Pt. 1),

G79-G91

CODEN: AJPHAP; ISSN: 0002-9513 American Physiological Society

DOCUMENT TYPE: Journal LANGUAGE: English ED Entered STN: 04 Feb 1999

AB The pathol. of Crohn's disease and ulcerative colitis is characterized by chronic inflammation and destruction of the gastrointestinal epithelium. Although suppression of inflammatory mediators remains the principal component of current disease therapeutics, strategies for enhancing repair and regeneration of the compromised intestinal epithelium have not been widely explored. The demonstration that a peptide hormone secreted by the intestinal epithelium, glucagon-like peptide-2 (GLP-2), is a potent endogenous stimulator of intestinal epithelial proliferation in the small bowel prompted studies of the therapeutic efficacy of GLP-2 in CD1 and BALB/c mice with dextran sulfate (DS)-induced colitis. The authors report that a human GLP-2 analog (h[Gly2]GLP-2) significantly reverses weight loss, reduces interleukin-1 expression, and increases colon length, crypt depth, and both mucosal area and integrity in the colon of mice with acute DS The effects of h[Gly2]GLP-2 in the colon are mediated in part via enhanced stimulation of mucosal epithelial cell proliferation. These observations suggest that exploitation of the normal mechanisms used to ... regulate intestinal proliferation may be a useful adjunct for healing

mucosal epithelium in the presence of active intestinal inflammation.

CC 2-6 (Mammalian Hormones)

IT Intestine

(colon, epithelium; human [Gly2]GLP-2 reduces severity of colonic injury in mice with dextran sulfate-induced colitis)

IT Intestine, disease

Intestine, disease

(colon, injury; human [Gly2]GLP-2 reduces severity of colonic injury in mice with dextran sulfate-induced colitis)

IT Intestine, disease

(ulcerative colitis; human [Gly2]GLP-2 reduces severity of colonic injury in mice with dextran sulfate-induced colitis)

IT 197922-42-2

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(human [Gly2]GLP-2 reduces severity of colonic injury in mice with dextran sulfate-induced colitis)

REFERENCE COUNT:

56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 19 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

1998:789042 CAPLUS

DOCUMENT NUMBER:

130:43339

TITLE:

Glucagon-like peptide 2 formulations for enhancing

functioning of the upper gastrointestinal

tract

INVENTOR (S):

Drucker, Daniel J.

PATENT ASSIGNEE(S):

1149336 Ontario Inc., Can.

SOURCE:

PCT Int. Appl., 64 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| | PATENT NO. | | | | | | | | | | LICAT | | | | | | |
|----------|--------------|-----------------|------|-----|-----|-----|------|------|-----|----|--------|------|-----|-----|-----|------|-----|
| | | | | | | | | | | | 1998-0 | | | | | | |
| | | | | | | | | | | | , BY, | | | | | | |
| | | | | | | | | | | | , HU, | | | | | | |
| | • | | | | | | | | | | , LV, | | | | | | |
| | | NO, | NZ, | PL, | PT, | RO, | RU, | SD, | SE, | SG | , SI, | SK, | SL, | ТJ, | TM, | TR, | TT, |
| | | | | | | | | | | | , KG, | | | | | | |
| | RW: | GH, | GM, | KE, | LS, | MW, | SD, | SZ, | UG, | ZW | , AT, | BE, | CH, | CY, | DE, | DK, | ES, |
| | | FI, | FR, | GB, | GR, | ΙE, | IT, | LU, | MC, | NL | , PT, | SE, | BF, | ВJ, | CF, | CG, | CI, |
| | • | CM, | GΑ, | GN, | ML, | MR, | NE, | SN, | TD, | TG | | | | | | | |
| US | 6051 | 557 | | | Α | | 2000 | 0418 | | US | 1998- | 5950 | 4 | | 1 | 9980 | 413 |
| CA | 2289 | 652 | | | AA | | 1998 | 1126 | | CA | 1998- | 2289 | 652 | | 1 | 9980 | 515 |
| | | | | | | | | | | AU | 1998- | 7516 | 3 | | 1 | 9980 | 515 |
| ·AU | 7466 | 33 | | | B2 | | 2002 | 0502 | | | | | | | | | |
| EP | 9813 | 62 | | | A1: | | 2000 | 0301 | | ΕP | 1998- | 9225 | 46 | | 1 | 9980 | 515 |
| EP | 9813 | | | | | | | | | | | | | | | | |
| | R: | ΑT, | BE, | CH, | DE, | DK, | ES, | FR, | GB, | GR | , IT, | LI, | LU, | NL, | SE, | MC, | PT, |
| | | ΙE, | | | | | | | | | | | | | | | |
| | 9808 | | | | Α | | | | | | 1998- | | | | | | |
| JP | 2002 2533 | 5023 | 69 | | T2 | | | | | | 1998- | | | | | | |
| AT | 2533 | 75 [°] | | | E | | | | | | 1998- | | | | | 9980 | |
| PT | 9813 | 62 | | | | | | | | | 1998- | | | | | | |
| ES | 2210 | 756 | | | Т3 | | 2004 | 0701 | | | 1998- | | | | | | |
| PRIORITY | Y APP | LN. | INFO | .: | | | | | | | 1997- | | | | | | |
| | | | | | | | | | | GB | 1997- | 1548 | 1 | | A 1 | 9970 | 723 |

US 1998-59504 A 19980413 WO 1998-CA497 W 19980515 ED Entered STN: 16 Dec 1998 AB The invention relates to glucagon-related peptides and their use for the prevention or treatment of disorders involving the upper gastrointestinal tract including the esophagus and stomach. In particular, it has now been demonstrated that GLP-2 and peptidic agonists of GLP-2 can cause proliferation of the tissue of the upper gastrointestinal tract. the invention provides methods of proliferating the upper gastrointestinal tract in a subject in need thereof. Further, the methods of the invention are useful to treat or prevent inflammatory conditions of the upper gastrointestinal tract, including inflammatory diseases. GLP-2 stimulates the growth of upper gastrointestinal tissue when administered in conjunction with other peptide hormones. The invention further provides pharmaceutical compns. of GLP-2 with at least one other peptide hormone, methods of enhancing the growth of upper gastrointestinal tissue and of gastrointestinal disorders by increasing serum levels of GLP-2 and at least one other peptide hormone, and kits for performing the methods of the invention. IC ICM A61K038-26 A61K038-30; A61K038-27; A61K035-38; G01N033-50; C12N005-06; C12N005-08; A61K038-30; A61K038-26; A61K038-27; A61K038-26; A61K038-26; A61K038-18 CC 63-6 (Pharmaceuticals) Section cross-reference(s): 2 ST glucagon like peptide 2 upper gastrointestinal tract IT Intestine, disease (Crohn's; glucagon-like peptide 2 formulations for enhancing functioning of the upper gastrointestinal tract) ITPeptides, biological studies RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (GLP-2 analogs; glucagon-like peptide 2 formulations for enhancing functioning of the upper gastrointestinal tract) IT Receptors RL: BSU (Biological study, unclassified); BIOL (Biological study) (GLP-2, agonists; glucagon-like peptide 2 formulations for enhancing functioning of the upper gastrointestinal tract) Esophagus TT (acid reflux; glucagon-like peptide 2 formulations for enhancing functioning of the upper gastrointestinal tract) ITStomach, disease (atrophic gastritis, metaplastic; glucagon-like peptide 2 formulations for enhancing functioning of the upper gastrointestinal tract) IT Stomach (bile reflux; glucagon-like peptide 2 formulations for enhancing functioning of the upper gastrointestinal tract) IT Sarcoidosis (esophageal; glucagon-like peptide 2 formulations for enhancing functioning of the upper gastrointestinal tract) IT Esophagus (esophagitis; glucagon-like peptide 2 formulations for enhancing functioning of the upper gastrointestinal tract) IT Stomach, disease (gastritis; glucagon-like peptide 2 formulations for enhancing functioning of the upper gastrointestinal tract)

(gastrointestinal injury from; glucagon-like peptide 2 formulations for enhancing functioning of the upper

IT

Radiotherapy

gastrointestinal tract)

```
IT
     Anti-inflammatory agents
     Behcet's syndrome
     Esophagus
     Genetic engineering
     Helicobacter pylori
       Stomach
        (qlucagon-like peptide 2 formulations for enhancing functioning of the
        upper gastrointestinal tract)
IT
     Hepatocyte growth factor
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); PEP (Physical, engineering or chemical process); THU
     (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
        (glucagon-like peptide 2 formulations for enhancing functioning of the
        upper gastrointestinal tract)
IT
     Transplant and Transplantation
        (graft-vs.-host reaction; glucagon-like peptide 2 formulations for
        enhancing functioning of the upper gastrointestinal tract)
IT
     Drug delivery systems
        (injections, i.v.; glucagon-like peptide 2 formulations for enhancing
        functioning of the upper gastrointestinal tract)
     Drug delivery systems
IT
        (injections, s.c.; glucagon-like peptide 2 formulations for enhancing
        functioning of the upper gastrointestinal tract)
IT
     Drug delivery systems
        (oral; glucagon-like peptide 2 formulations for enhancing functioning
        of the upper gastrointestinal tract)
IT
     Surgery
        (resection, of upper gastrointestinal tract; glucagon-like
        peptide 2 formulations for enhancing functioning of the upper
        gastrointestinal tract)
TT.
     Cell proliferation.
        (stimulation of; glucagon-like peptide 2 formulations for enhancing
        functioning of the upper gastrointestinal tract)
IT
     Digestive tract
        (upper; glucagon-like peptide 2 formulations for enhancing functioning
        of the upper gastrointestinal tract)
     9002-72-6, Somatotropin 9002-72-6D, Somatotropin, analogs
                                                                    67763-96-6,
IT,
             67763-97-7, Igf-2 148348-15-6, Fibroblast growth factor 7
     Iqf-1
     197922-42-2
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); PEP (Physical, engineering or chemical process);
     THU (Therapeutic use); BIOL (Biological study); PROC (Process);
     USES (Uses)
        (glucagon-like peptide 2 formulations for enhancing functioning of the
        upper gastrointestinal tract)
     89750-15-2, Glucagon-like peptide 2
IT
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); PEP (Physical, engineering or chemical process); THU
     (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
        (receptors, agonists; glucagon-like peptide 2 formulations for
        enhancing functioning of the upper gastrointestinal tract)
                               THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS
REFERENCE COUNT:
                         6
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
L46 ANSWER 20 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:
                         1998:402335 CAPLUS
DOCUMENT NUMBER:
                         129:77032
TITLE:
                         Compositions containing glucagon-related peptides in
                         combination with other agents for enhancing intestinal
                         function
                         Drucker, Daniel J.
INVENTOR(S):
```

PATENT ASSIGNEE(S):

1149336 Ontario Inc., Can.; Drucker, Daniel J.

SOURCE:

PCT Int. Appl., 44 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

| | | | | | | | | | | | LICAT: | | | | | ATE | |
|---------|------|-----|------|-----|-----|-----|------|------|-----|------|--------|------|------|-----|------------|-------|-----|
| | | | | | | - | | | | | | | | | - | | |
| WO | 9825 | 644 | | | A1 | | 1998 | 0618 | 1 | WO 1 | L997-0 | CA94 | 5 | | 1 | 9971: | 210 |
| | W: | ΑL, | AM, | ΑT, | ΑU, | ΑZ, | BA, | BB, | BG, | BR, | BY, | CA, | CH, | CN, | CU, | CZ, | DE, |
| | | DK, | EE, | ES, | FI, | GB, | GE, | GH, | GM, | HU, | ID, | IL, | IS, | JP, | KΕ, | KG, | KP, |
| | | KR, | ΚZ, | LC, | LK, | LR, | LS, | LT, | LU, | LV, | MD, | MG, | MK, | MN, | MW, | MX, | NO, |
| | | NZ, | PL, | PT, | RO, | RU, | SD, | SE, | SG, | SI, | SK, | SL, | TJ, | TM, | TR, | TT, | UA, |
| | | ŪĠ, | US, | UZ, | VN, | YU, | ZW, | AM, | AZ, | BY, | KG, | KZ, | MD, | RU, | TJ, | TM | |
| | RW: | GH, | GM, | KE, | LS, | MW, | SD, | SZ, | UG, | ZW, | AT, | BE, | CH, | DE, | DK, | ES, | FI, |
| | | FR, | GB, | GR, | ΙE, | IT, | LU, | MC, | NL, | PT, | SE, | BF, | ВJ, | CF, | CG, | CI, | CM, |
| | | GA, | GN, | ML, | MR, | NE, | SN, | TD, | TG | | | | | | | | |
| US | 5952 | 301 | | | Α | | 1999 | 0914 | 1 | US 1 | L996-' | 7631 | 77 | | 1 | 9961 | 210 |
| | | | | | | | | | | | L997-: | | | | | | |
| | 2274 | | | | | | | | | | | | | | | | |
| AU | 9852 | 200 | | | A1 | | 1998 | 0703 | | AU 1 | L998-! | 5220 | 0 | | 1 | 9971 | 210 |
| EP | 9443 | 96 | | | A1 | | 1999 | 0929 | | EP 1 | L997- | 9469 | 86 | | 1 | 9971 | 210 |
| EP | 9443 | 96 | | | B1 | | 2003 | 0226 | | | | | | | | | |
| | R: | ΑT, | BE, | CH, | DE, | DK, | ES, | FR, | GB, | GR, | IT, | LI, | LU, | NL, | SE, | MC, | PT, |
| | | ΙE, | FI | | | | | | | | | | | | | | |
| AT | 2330 | 96 | | | E | | 2003 | 0315 | | AT 1 | 1997- | 9469 | 86 | | 1 | 9971: | 210 |
| | 9443 | | | | | | 2003 | 0731 | | PT 1 | L997- | 9469 | 86 | | 1 | 9971 | 210 |
| ES | 2193 | 406 | | | Т3 | | 2003 | 1101 | | ES 1 | L997- | 9469 | 86 , | | 1 | 9971: | 210 |
| PRIORIT | APP | LN. | INFO | .: | | | | | | US 1 | 1996- | 7631 | 77 | i | A 1 | 9961 | 210 |
| | | | | | | | | | 1 | WO 1 | L997-0 | CA94 | 5 | 1 | 1 | 9971 | 210 |

ED Entered STN: 01 Jul 1998

GLP-2 stimulates the growth of both small intestine and large intestine AB tissue when administered in conjunction with other agents. The invention provides pharmaceutical compns. of GLP-2 with at least one other agent that increase the biol. activity of GLP-2, methods of enhancing the growth of both small and large intestine tissue and of ameliorating nutritional or gastrointestinal disorders by increasing serum levels of GLP-2 and at least one other agent, and kits for performing the methods of the invention.

IC ICM A61K038-30

ICS A61K038-27; A61K038-26; C12N005-06; C12N005-08; A61K038-30; A61K038-26; A61K038-27; A61K038-26; A61K038-26; A61K038-05

2-6 (Mammalian Hormones) CC

Section cross-reference(s): 63

IT Digestive tract

Endocrine system

(disease; compns. containing glucagon-related peptides in combination with other agents for enhancing intestinal function)

IT Intestine, disease

> (enteritis; compns. containing glucagon-related peptides in combination with other agents for enhancing intestinal function)

ITIntestine, disease

(infarction; compns. containing glucagon-related peptides in combination with other agents for enhancing intestinal function)

IT Intestine, disease

> (inflammatory; compns. containing glucagon-related peptides in combination with other agents for enhancing intestinal function)

ITIntestine, disease

(large; compns. containing glucagon-related peptides in combination with other agents for enhancing intestinal function)

IT Intestine, disease

(malabsorption; compns. containing glucagon-related peptides in combination with other agents for enhancing intestinal function)

IT Intestine, disease

(post-infectious villous atrophy; compns. containing glucagon-related peptides in combination with other agents for enhancing intestinal function)

IT Intestine, disease

(short bowel syndrome; compns. containing glucagon-related peptides in combination with other agents for enhancing intestinal function)

Intestine, disease TT

Intestine, disease

(small; compns. containing glucagon-related peptides in combination with other agents for enhancing intestinal function)

9002-72-6D, GH, analogs 9002-72-6, GH 12629-01-5, Human growth hormone 67763-96-6, IGF-1 67763-96-6D, IGF-1, analogs 67763-97-7, IGF 2 67763-97-7D, IGF 2, analogs 89750-15-2, Glucagon-like peptide-2 89750-15-2D, Glucagon-like peptide 2, analogs 93927-39-0, Glucagon-related peptide II (rat) 99120-49-7, Glucagon-related peptide II (human) 133745-65-0 143045-27-6 197922-63-7 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(compns. containing glucagon-related peptides in combination with other agents for enhancing intestinal function)

REFERENCE COUNT:

THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 21 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN

8

ACCESSION NUMBER:

1998:394356 CAPLUS

DOCUMENT NUMBER:

129:62975

TITLE:

Use of keratinocyte growth factors and glucagon-like

peptide 2 to increase proliferation and/or differentiation of epithelial cells of

gastrointestinal tract

INVENTOR(S):

Farrell, Catherine L.; Li, Yue-Sheng

PATENT ASSIGNEE(S):

Amgen Inc., USA; Farrell, Catherine L.; Li, Yue-Sheng

SOURCE: PCT Int. Appl., 158 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

| PAT | CENT 1 | | KINI |) | DATE | | | APPL: | | | | | DA | ATE | | | |
|-----|--------|-----|------|-----|------------|-----|------|-------|-----|-------|-------|-------|-----|-----|-----|-------|-----|
| | 9824 | | | | | | 1998 | | | | | | | | 19 | 99712 | 208 |
| WO | 9824 | 813 | | | A 3 | | 1998 | 0806 | | | | | | | | | |
| | W: | AL, | AM, | ΑT, | AU, | ΑZ, | BA, | BB, | BG, | BR, | BY, | CA, | CH, | CN, | CU, | CZ, | DE, |
| | | DK, | EE, | ES, | FΙ, | GB, | GE, | GH, | HU, | ID, | IL, | IS, | JΡ, | KE, | KG, | KP, | KR, |
| | | | | | | | LT, | | | | | | | | | | |
| | | PL, | PT, | RO, | RU, | SD, | SE, | SG, | SI, | SK, | SL, | TJ, | TM, | TR, | TT, | UA, | UG, |
| | | US, | UZ, | VN, | YU, | ZW, | AM, | AZ, | BY, | KG, | KZ, | MD, | RU, | TJ, | .TM | · | , |
| | RW: | GH, | KE, | LS, | MW, | SD, | SZ, | UG, | ZW, | AT, | BE, | CH, | DE, | DK, | ES, | FI, | FR, |
| | | | | | | | MC, | | | | | | | | | | |
| | | GN, | ML, | MR, | ΝE, | SN, | TD, | TG | | | | | | | | | |
| CA | 2272 | 854 | | | AA | | 1998 | 0611 | (| CA 19 | 997-2 | 22728 | 354 | | 19 | 9712 | 208 |
| CA | 2272 | 854 | | | C | | 2004 | 0210 | | | | | | | | | |
| ΑU | 9856 | 962 | | | A1 | | 1998 | 0629 | 7 | AU 19 | 998-5 | 56962 | 2 | | 19 | 9712 | 208 |
| ΕP | 1012 | 186 | | | A2 | | 2000 | 0628 | 1 | EP 19 | 997-9 | 9531 | 57 | | 19 | 9712 | 208 |
| ΕP | 1012 | 186 | | | В1 | | 2002 | 0717 | | | | | | | | | |
| | R: | AT, | ΒE, | CH, | DE, | DK, | ES, | FR, | GB, | GR, | IT, | LI, | LU, | NL, | SE, | MC, | PT, |
| | | | | LT, | | | | | | | | | | | | | |

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JP 2001510333
                          T2
                                20010731
                                            JP 1998-525894
                                                                    19971208
                          E
                                20020815
                                            AT 1997-953157
                                                                    19971208
    AT 220689
                          Т3
                                20030216
                                            ES 1997-953157
                                                                    19971208
    ES 2181054
    MX 9905163
                          Α
                                20000228
                                            MX 1999-5163
                                                                    19990603
                                                                P 19961206
PRIORITY APPLN. INFO.:
                                            US 1996-32533P
                                            US 1997-62074P
                                                                P 19971015
                                            WO 1997-US22735
                                                                W 19971208
    Entered STN: 27 Jun 1998
ΑB
    The combined use of KGF variants and GLP-2 to increase proliferation
     and/or differentiation of epithelial cells of gastrointestinal tract, especially
     to treat chemotherapy-related mucositis, is disclosed. The effects of KGF
     and GLP-2 are synergistic.
TC
    ICM C07K014-00
     ICS
         C07K014-605; A61K038-18
CC
    1-9 (Pharmacology)
    gastrointestinal epithelium growth differentiation KGF GLP2;
ST
     keratinocyte growth factor GLP2 gastrointestinal epithelium;
    glucagon like peptide 2 KGF gastrointestine; mucositis
    chemotherapy KGF GLP2
    Mucous membrane
TT
        (disease, inflammation, treatment of
        chemotherapy-induced; use of keratinocyte growth factors and
        glucagon-like peptide 2 to increase proliferation and/or
        differentiation of epithelial cells of gastrointestinal
        tract)
    Mucous membrane
TT
        (inflammation, treatment of chemotherapy-induced; use of
        keratinocyte growth factors and glucagon-like peptide 2 to increase
        proliferation and/or differentiation of epithelial cells of
        gastrointestinal tract)
    Cell differentiation
TT
    Cell proliferation
       Digestive tract
    Epithelium
        (use of keratinocyte growth factors and glucagon-like peptide 2 to
        increase proliferation and/or differentiation of epithelial cells of
        gastrointestinal tract)
                                               178236-44-7
TT
     162394-19-6
                  178236-42-5
                                 178236-43-6
                                                             178236-45-8
                                               208879-42-9
                                                             208879-43-0
    208879-39-4
                   208879-40-7
                                 208879-41-8
                                 208879-46-3
                                               208879-47-4
                                                             208879-48-5
                   208879-45-2
    208879-44-1
                   208879-50-9
    208879-49-6
    RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES
     (Uses)
        (amino acid sequence; use of keratinocyte growth factors and
        glucagon-like peptide 2 to increase proliferation and/or
        differentiation of epithelial cells of gastrointestinal
        tract)
IT
    197922-42-2 197922-45-5
    RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological
    study); USES (Uses)
        (use of keratinocyte growth factors and glucagon-like peptide 2 to
        increase proliferation and/or differentiation of epithelial cells of
        gastrointestinal tract)
    99120-49-7, Glucagon-related peptide II (human)
IT
                                                       126469-10-1D,
    Fibroblast growth factor 7 (human clone 32/49 protein moiety reduced),
    variants
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (use of keratinocyte growth factors and glucagon-like peptide 2 to
        increase proliferation and/or differentiation of epithelial cells of
        gastrointestinal tract)
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ACCESSION NUMBER:
```

1998:163617 CAPLUS

DOCUMENT NUMBER:

128:230696

TITLE:

Preparation of lipophilic derivatives of human

glucagon-like peptide-2 (hGLP-2)

INVENTOR(S):

Knudsen, Liselotte Bjerre; Sorensen, Per Olaf;

Nielsen, Per Franklin

PATENT ASSIGNEE(S):

Novo Nordisk A/S, Den.; Knudsen, Liselotte Bjerre;

Sorensen, Per Olaf; Nielsen, Per Franklin

SOURCE:

PCT Int. Appl., 26 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

12

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

| | PAT | ENT 1 | | | | | | | | | APPL | ICAT | ION I | NO. | | Ι | ATE | | | | |
|-------|--------|--------------|-------|-----|-------|-----|------|----------|------|-----|------|-----------|-------|-----|-----|------------|-------|-----|-------|------|--|
| | WO | 98088 | | | | | | 1998 | | | WO 1 | 997-: | DK36 | 0 | |] | .9970 | 901 | | | |
| | | | | | | | | | | | | | | | | | CZ, | DE, | | | |
| | | | | | | | | | | | | | | | | | KR, | | | | |
| | | | | | | | | | | | | | | | | | NZ, | | | | |
| | | | | | | | | | | | | | | | | | UG, | | | | |
| | | | | | | | | | | | KZ, | | | | | | • | • | | | |
| | | pw. | | | | | | | | | | | | | | ES. | FI, | FR, | | | |
| | | 1011. | GR | GR | IE. | TT. | LII. | MC. | NI. | PT. | SE. | BF. | ВJ. | CF. | CG, | CI | CM, | GA, | | | |
| | | | | | | | | TD, | | , | , | | • | • | • | | | | | | |
| | ďΡ | 2001 | | | | | | | | | JP 2 | 000- | 1527 | 78 | | - | 9970 | 822 | | | |
| | | 9707 | | | | | | | | | | | | | | | 9970 | | | | |
| | 7.A | 9707 | 828 | | | A | | 1998 | 0302 | | ZA 1 | 997- | 7828 | | | - | 9970 | 901 | | | |
| | ΔIJ | 9707 9741 | 124 | | | A1 | | 1998 | 0319 | | AU 1 | 997- | 4112 | 4 | | : | 9970 | 901 | | | |
| | EP | 9295 | 76 | | | A1 | | 1999 | 0721 | | EP 1 | 997- | 9388 | 02 | | : | 9970 | 901 | | | |
| | | | | | | | | | | | | | | | | | PT, | | - | | |
| | | | | LT, | | | | | · | | | | | | | | | | | | |
| | JP | 2000 | 5173 | 08 | | Т2 | | 2000 | 1226 | | JP 1 | 998- | 5111 | 93 | | | L9970 | 901 | | | |
| | US | 2002 | 0259 | 33 | | A1 | | 2002 | 0228 | | US 2 | 001- | 9085 | 34 | | 2 | 20010 | 718 | | | |
| | US | 2004 | 1274 | 18 | | A1 | | 2004 | 0701 | | US 2 | 003- | 7302 | 15 | | : | 20031 | 208 | | | |
| PRIOR | | | | | | | | | | | | | | | | | L9960 | | | | |
| | | | | | | | | | | | DK 1 | 996- | 1259 | | | A : | 19961 | 108 | | | |
| | | | | | | | | | | | DK 1 | 996- | 1470 | | | A : | 19961 | 220 | | | |
| | | | | | | | | | | | US 1 | 997- | 3590 | 5P | | P : | L9970 | 124 | | | |
| | | | | | | | | | | | | | | | | P : | L9970 | 125 | | | |
| | | | | | | | | | | | JP 1 | 998- | 5111 | 83 | | A3 | L9970 | 822 | | | |
| | | | | | | | | | | | WO 1 | 997- | DK36 | 0 | | W : | L9970 | 901 | | | |
| | | | | | | | | | | | US 1 | 997- | 9222 | 00 | | B2 : | L9970 | 902 | | | |
| | | | | | | | | | | | DK 1 | 998~ | 271 | | | A : | L9980 | 227 | | | |
| | | | | | | | | | | | | | | | | P : | 19980 | 518 | | | |
| | | | | | | | | | | | US 1 | .999- | 2581 | 87 | | B1 | 19990 | 225 | | | |
| | | | | | | | | | | | US 2 | 001- | 9085 | 34 | | A1 : | 20010 | 718 | | | |
| === | | | COUNT | | 0 14- | 10 | 00 | | | | | | | | | | | | | | |

Entered STN: 19 Mar 1998 ED

Derivs. of hGLP-2 (H-His-Ala-Asp-Gly-Ser-Phe-Ser-Asp-Glu-Met-Asn-Thr-Ile-AB Leu-Asp-Asn-Leu-Ala-Ala-Arg-Asp-Phe-Ile-Asn-Trp-Leu-Ile-Gln-Thr-Lys-Ile-Thr-Asp-Arg-OH), where a lipophilic substituent (such as an acyl group of a straight-chain or branched fatty acid) is attached to any one amino acid residue, are claimed. For example, Lys30(Nɛ-tetradecanoyl)hGLP-2 was synthesized in 47% yield from the reactants hGLP-2 and tetradecanoic acid hydroxysuccinimide ester in the presence of N-ethyl-N,Ndiisopropylamine (EDPA) and N-methyl-2-pyrrolidone (NMP). The titled compds. can be used in the treatment of obesity, small bowel syndrome, etc. (no data).

ICM C07K014-605 TC

ICS A61K038-26

CC 34-3 (Amino Acids, Peptides, and Proteins)

```
Section cross-reference(s): 1, 2
    Intestine, disease
IT
        (use of lipophilic derivs. of hGLP-2 for treatment of small bowel
        syndrome)
     99120-49-7DP, Glucagon-related peptide II (human), derivs.
IT
     204319-62-0DP, 1-30-Glucagon-related peptide II (human), derivs.
     204319-64-2DP, 1-31-Glucagon-related peptide II (human), derivs.
     204401-90-1DP, 1-32-Glucagon-related peptide II (human), derivs.
     204401-91-2P 204401-92-3P 204401-93-4P
     204401-94-5P 204401-95-6P 204401-96-7P
     204401-97-8P 204401-98-9P 204401-99-0P
     204402-00-6P 204402-01-7P 204402-02-8P
     204402-03-9P 204402-04-0P 204402-05-1P
     204402-06-2P 204402-07-3P 204402-08-4P
     204402-09-5P 204402-10-8P 204461-70-1P
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU (Therapeutic
     use); BIOL (Biological study); PREP (Preparation); USES (Uses)
        (preparation of lipophilic derivs. of hGLP-2)
     69888-86-4 99120-49-7, Glucagon-related peptide II (human)
IT
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (preparation of lipophilic derivs. of hGLP-2)
                               THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS
REFERENCE COUNT:
                         3
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
L46 ANSWER 23 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN
                         1998:89268 CAPLUS
ACCESSION NUMBER:
DOCUMENT NUMBER:
                         128:154390
                         Preparation and agonistic and antagonistic activity of
TITLE:
                         glucagon-like peptide 2 analogs
                         Drucker, Daniel J.; Crivici, Anna E.; Sumner-Smith,
INVENTOR (S):
                         Martin
                         1149336 Ontario Inc., Can.; Allelix Biopharmaceuticals
PATENT ASSIGNEE(S):
                         Inc.; Drucker, Daniel J.; Crivici, Anna E.;
                         Sumner-Smith, Martin
                         PCT Int. Appl., 40 pp.
SOURCE:
                         CODEN: PIXXD2
DOCUMENT TYPE:
                         Patent
LANGUAGE:
                         English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:
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| PA | FENT | | | | | | | | | | ICAT | | | | | | | |
|----|------|------|-----|-----|-----|-----|------|------|-----|------|------|-------|-----|-----|-----|-------|-----|--|
| | | | | | | | | | | | | | | | | | | |
| WO | 9803 | 547 | | | A1 | | 1998 | 0129 | 1 | WO 1 | 997- | CA52 | 1 | | 19 | 9970' | 718 | |
| | W: | AL, | AM, | AT, | AU, | ΑZ, | BA, | BB, | BG, | BR, | BY, | CA, | CH, | CN, | CU, | CZ, | DE, | |
| | | DK, | EE, | ES, | FI, | GB, | GE, | GH, | HU, | ΙL, | IS, | JP, | KΕ, | KG, | KΡ, | KR, | KZ, | |
| | | LC, | LK, | LR, | LS, | LT, | LU, | LV, | MD, | MG, | MK, | MN, | MW, | MX, | NO, | NZ, | PL, | |
| | | PT, | RO, | RU, | SD, | SE, | SG, | SI, | SK, | SL, | ТJ, | TM, | TR, | TT, | UA, | UG, | US, | |
| | | UΖ, | VN, | YU, | ZW, | AM, | ΑZ, | BY, | KG, | KZ, | MD, | RU, | TJ, | TM | | | | |
| | RW: | GH, | KE, | LS, | MW, | SD, | SZ, | UG, | ZW, | ΑT, | BE, | CH, | DE, | DK, | ES, | FI, | FR, | |
| | | GB, | GR, | IE, | IT, | LU, | MC, | NL, | PT, | SE, | BF, | ВJ, | CF, | CG; | CI, | CM, | GA, | |
| | | GN, | ML, | MR, | ΝE, | SN, | TD, | TG | | | | | | | | | | |
| US | 5994 | 500 | | | Α | | 1999 | 1130 | 1 | US 1 | 996- | 6838 | 90 | | 1: | 9960' | 719 | |
| CA | 2260 | 291 | | | AA | | 1998 | 0129 | (| CA 1 | 997- | 2260 | 291 | | 1 | 9970 | 718 | |
| ΑU | 9736 | 157 | | | A1 | | 1998 | 0210 | i | AU 1 | 997- | 3615 | 7 | | 1 | 9970 | 718 | |
| ΑU | 7392 | 63 | | | B2 | | 2001 | 1011 | | | | | | | | | | |
| EP | 9143 | 41 | | | A1 | | 1999 | 0512 |] | EP 1 | 997- | 9326' | 72 | | 19 | 9970 | 718 | |
| | R: | ΑT, | BE, | CH, | DE, | DK, | ES, | FR, | GB, | GR, | IT, | LI, | LU, | NL, | SE, | MC, | PT, | |
| | | ΙE, | FΙ | | | | | | | | | | | | | | | |
| JP | 2000 | 5165 | 79 | | T2 | | 2000 | 1212 | , | JP 1 | 998- | 5064 | 09 | | 1 | 9970 | 718 | |
| US | 6489 | 295 | | | B1 | | 2002 | 1203 | 1 | US 1 | 999- | 2339 | 34 | | 1: | 9990 | 119 | |

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US 2003109449
                          Α1
                                20030612
                                            US 2002-295820
                                                                    20021118
PRIORITY APPLN. INFO.:
                                            US 1996-683890
                                                                 A 19960719
                                            WO 1997-CA521
                                                                 W 19970718
                                            US 1999-233934
                                                                 A3 19990119
ED
     Entered STN: 16 Feb 1998
     Antagonists of glucagon-like peptide 2, H-His-Ala-Asp-Gly-Ser-Phe-Ser-Asp-
AB
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Glu-Met-Asn-Thr-Ile-Leu-Asp-Asn-Leu-Ala-Ala-Arg-Asp-Phe-Ile-Asn-Trp-Leu-Ile-Gln-Thr-Lys-Ile-Thr-Asp-Arg-OH (GLP-2), have been identified. Their effects on the growth of gastrointestinal tissue are described. Its formulation as a pharmaceutical, and its therapeutic and related uses in treating bowel tissue, are described. Also described are methods of identifying antagonists of glucagon-like peptide 2. Thus, [Glu2]-GLP-2, prepared by standard solid-phase methods using Merrifield resin and tert-butoxycarbonyl (Boc) protection, showed a 25% decrease in small bowel weight in a CD1 mouse assay.

IC ICM C07K014-605

ICS A61K038-26; G01N033-68

CC 34-3 (Amino Acids, Peptides, and Proteins) Section cross-reference(s): 1

IT Intestine, disease

> (irritable bowel syndrome; preparation and agonistic and antagonistic activity of glucagon-like peptide 2 analogs)

IT 99120-49-7DP, Glucagon-related peptide II (human), analogs

197664-36-1P 197922-12-6P 197922-35-3P 197922-54-6P 202533-93-5P

202533-95-7P 202606-11-9P 202606-13-1P 202606-14-2P

202606-15-3P 202606-16-4P 202606-17-5P 202606-18-6P

202606-19-7P 202606-20-0P 202606-21-1P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation and agonistic and antagonistic activity of glucagon-like peptide 2 analogs)

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 24 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN ACCESSION NUMBER:

1999:407767 CAPLUS

DOCUMENT NUMBER:

REFERENCE COUNT:

131:28314

TITLE:

Methods of enhancing functioning of the large

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS

intestine with glucagon-related peptides

INVENTOR(S): Drucker, Daniel J.

PATENT ASSIGNEE(S):

1149336 Ontario Inc., Can.

SOURCE:

Can. Pat. Appl., 36 pp.

CODEN: CPXXEB

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| KIND | DATE | APPLICATION NO. | | DATE |
|------|----------|-----------------|-----------------------------|-----------------------------|
| | | | | |
| AA | 19981102 | CA 1998-2236519 | | 19980504 |
| | | US 1997-850664 | Α | 19970502 |
| | | | AA 19981102 CA 1998-2236519 | AA 19981102 CA 1998-2236519 |

Entered STN: 02 Jul 1999 ED

The invention relates to glucagon-related peptides and their use for the AB prevention or treatment of disorders involving the large intestine. In particular, it has now been demonstrated that GLP-2 and peptidic agonists of GLP-2 can cause proliferation of the tissue of large intestine. Thus, the invention provides methods of proliferating the large intestine in a subject in need thereof. Further, the methods of the invention are useful to treat or prevent inflammatory conditions of the large intestine, including inflammatory bowel diseases. Methods for identifying peptides

useful to treat inflammatory conditions involving the large intestine are also claimed.

IC ICM A61K038-26

ICS C12Q001-00; G01N033-483

CC 2-6 (Mammalian Hormones)

IT Intestine, disease

(Crohn's; GLP-2 and its analogs for the treatment or prevention of inflammatory conditions of the large intestine)

IT Gastrointestinal hormone receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study) (GLP-2 receptors, agonists; GLP-2 and its analogs for the treatment or prevention of inflammatory conditions of the large intestine)

IT Intestine, disease

(colitis, ischemic and infectious and drug or chemical induced; GLP-2 and its analogs for the treatment or prevention of **inflammatory** conditions of the large intestine)

IT Intestine, disease

(diverticulitis; GLP-2 and its analogs for the treatment or prevention of inflammatory conditions of the large intestine)

IT Intestine, disease

(inflammatory; GLP-2 and its analogs for the treatment or prevention of inflammatory conditions of the large intestine)

IT Intestine

(large; GLP-2 and its analogs for the treatment or prevention of inflammatory conditions of the large intestine)

IT Intestine

(resection; GLP-2 and its analogs for the treatment or prevention of inflammatory conditions of the large intestine after resection)

IT Intestine, disease

(ulcerative colitis; GLP-2 and its analogs for the treatment or prevention of inflammatory conditions of the large intestine)

IT 89750-15-2, Glucagon-like peptide II 89750-15-2D, Glucagon-like peptide II, analogs 195262-56-7 197664-29-2

197922-42-2 197922-60-4 197923-49-2

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(GLP-2 and its analogs for the treatment or prevention of inflammatory conditions of the large intestine)

L46 ANSWER 25 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:696789 CAPLUS

DOCUMENT NUMBER: 127:327015

TITLE: Glucagon-like peptide-2 analogs

INVENTOR(S): Drucker, Daniel J.; Crivici, Anna E.; Sumner-smith,

Martin

PATENT ASSIGNEE(S): 1149336 Ontario Inc., Can.; Allelix Biopharmaceuticals

Inc.

SOURCE: PCT Int. Appl., 38 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

| PATENT NO. | | | | KIND DATE | | | APPLICATION NO. | | | | | DATE | | | | | |
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| | | | | | - | | | | | | | | | | | | |
| WO 9739031 | | | | | A1 | A1 19971023 | | | 1 | WO 1997-CA252 | | | | | 19970411 | | |
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| | | LK, | LR, | LS, | LT, | LU, | LV, | MD, | MG, | MK, | MN, | MW, | MX, | NO, | NZ, | PL, | PT, |
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             IE, FI
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                                                                  A 19960412
PRIORITY APPLN. INFO.:
                                             WO 1997-CA252
                                                                  W 19970411
                                             EP 1997-916280
                                                                  A3 20011207
ED
     Entered STN: 05 Nov 1997
     Analogs of glucagon-like peptide-2, a product of glucagon gene expression,
AB
     have been identified as intestinal tissue growth factors. Their
     formulation as pharmaceutical and therapeutic use in treating disorders of
     the small bowel are described.
IC
     ICM C07K014-605
     ICS A61K038-26; G01N033-68
     2-2 (Mammalian Hormones)
CC.
     Section cross-reference(s): 34, 63
IT
     Intestine, disease
        (Crohn's; glucagon-like peptide-2 analogs)
IT
     Digestive tract
        (disease; glucagon-like peptide-2 analogs)
IT
     Intestine
     Ulcer
        (glucagon-like peptide-2 analogs)
IT
     Intestine, disease
        (inflammatory; glucagon-like peptide-2 analogs)
IT
     Intestine, disease
        (malabsorption; glucagon-like peptide-2 analogs)
IT
     Intestine, disease
        (short bowel syndrome; glucagon-like peptide-2 analogs)
                                  197664-23-6P
IT
     184378-22-1P 184378-24-3P
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                                    197664-26-9P
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     197664-24-7P
     197664-28-1P 197664-29-2P 197664-30-5P
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                    197664-33-8P
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197923-56-1P
             197923-57-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic
use); BIOL (Biological study); PREP (Preparation); USES (Uses)
   (glucagon-like peptide-2 analogs)
```

L46 ANSWER 26 OF 38 CAPLUS COPYRIGHT 2004 ACS on STN

1996:756228 CAPLUS ACCESSION NUMBER:

126:19330 DOCUMENT NUMBER:

Preparation of glucagon-like peptide-2 analogs as as TITLE:

gastrointestinal tissue growth factors

Drucker, Daniel J. INVENTOR(S):

1149336 Ontario Inc., Can. PATENT ASSIGNEE(S):

PCT Int. Appl., 55 pp. SOURCE:

CODEN: PIXXD2

Patent DOCUMENT TYPE: English LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION: DATENT NO

| | | | | | | | | APPLICATION NO. | | | | | | | | | |
|-----------|-----------|-------------|-----|-----|---------|-----|-------------------|-----------------|-----|----|-------|------|-----|-----|-----|------|-----|
| | | | | | | | WO 1996-CA232 | | | | | | | | | | |
| WO | | | | | | | | | | | | | | | | | |
| | W: | AL, | AM, | ΑT, | AU, | ΑZ, | BB, | BG, | BR, | BY | , CA, | CH, | CN, | CZ, | DE, | DK, | EE, |
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| | | LU. | LV. | MD. | MG. | MK, | MN. | MW. | MX. | NC | , NZ, | PL, | PT, | RO, | RU, | SD, | SE, |
| | | SG, | SI | · | • | · | • | • | • | | | • | • | • | • | • | • |
| | RW: | • | | MW, | SD, | SZ, | UG, | AT, | BE, | CH | , DE, | DK, | ES, | FI, | FR, | GB, | GR, |
| | | IE, | IT, | LU, | MC, | NL, | PT, | SE, | BF, | ΒJ | CF, | CG, | CI, | CM, | GA, | GN, | ML |
| US | 5990 | 07 7 | · | - | Α | | 1999 | 1123 | 1 | US | 1995- | 4225 | 40 | | 1 | 9950 | 414 |
| CA | 2218 | 225 | | | AA | | 1996 | 1017 | (| CA | 1996- | 2218 | 225 | | 1 | 9960 | 412 |
| AU | 9652 | 658 | | | A1 | | 1996 | 1030 | 1 | ΑU | 1996- | 5265 | 8 | | 1 | 9960 | 412 |
| AU | 7204 | 93 | | | B2 | | 2000 | 0601 | | | | | | | | | |
| EP | 8303 | 77 | | | A1 | | 19980 | 0325 |] | ΕP | 1996- | 9089 | 73 | | 1 | 9960 | 412 |
| | | | | | | | | | | | , IT, | | | | | | |
| | | IE, | FI | | | | | | | | | | | | | | |
| CN | 1188 | 485 | | | Α | | 19980 | 0722 | (| CN | 1996- | 1946 | 93 | | 1 | 9960 | 412 |
| | 1150 | | | | | | 19990 | 0521 | | JP | 1996- | 5306 | 06 | | 1 | 9960 | 412 |
| | | | | | | | 2002 | 1031 | 1 | ΑU | 2001- | 6556 | 6 | | 2 | 0010 | 830 |
| PRIORITY | | | | | | | | | | | 1995- | | | | | | |
| | - | | | | | | | | | | 1996- | | | | | 9960 | |
| OFFIED 01 | | (0) | | | 143 D.F | 3 m | 100 | 1022 | | | | | _ | | - | | |

OTHER SOURCE(S): MARPAT 126:19330

Entered STN: 26 Dec 1996 ED

- ΑB Glucagon-like peptide-2, a product of glucagon gene expression, and analogs of glucagon-like peptide-2, have been identified as gastrointestinal tissue growth factors. Their effects on the growth of small bowel and pancreatic islets are described. Their formulation as a pharmaceutical, and their therapeutic use in treating disorders of the bowel, are described. Thus, rat glucagon-like peptide-2, prepared by standard solid-phase methods using Boc chemical on a 4-methylbenzhydrylamine (MBHA) resin, administered for 10 days, stimulated villus elongation in CD1 mice small bowel. Proliferation rates in the proximal jejunum of the treated mice were increased 124% over control mice.
- ICM C07K014-605 IC ICS A61K038-26
- 34-3 (Amino Acids, Peptides, and Proteins) CC Section cross-reference(s): 1
- glucagon like peptide prepn gastrointestinotrophic; small bowel ST growth glucagon like peptide; pancreatic islet growth glucagon like

peptide

IT Digestive tract

(disease; preparation of glucagon-like peptide-2 analogs as as gastrointestinal tissue growth factors)

IT Pancreatic islet of Langerhans

(preparation of glucagon-like peptide-2 analogs as as gastrointestinal tissue growth factors)

IT Intestine

(small; preparation of glucagon-like peptide-2 analogs as as gastrointestinal tissue growth factors)

IT 89750-15-2P, Glucagon-related peptide-II

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(degu; preparation of glucagon-like peptide-2 analogs as as gastrointestinal tissue growth factors)

IT 93927-39-0P, Glucagon-related peptide II (rat) 99120-49-7P
, Glucagon-like peptide II (human) 107444-51-9P 184378-22-1P
184378-24-3P 184378-25-4P 184378-26-5P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of glucagon-like peptide-2 analogs as as

gastrointestinal tissue growth factors)

IT 71567-77-6, Glicentin

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(rat; preparation of glucagon-like peptide-2 analogs as as
qastrointestinal tissue growth factors)

L46 ANSWER 27 OF 38 USPATFULL on STN

ACCESSION NUMBER:

2004:165928 USPATFULL

TITLE:

GLP-2 derivatives

INVENTOR(S):

Knudsen, Liselotte Bjerre, Valby, DENMARK
Huusfeldt, Per Olaf, Kobenhavn K, DENMARK
Nielsen, Per Franklin, Varlose, DENMARK
Kaarsholm, Niels C., Vanlose, DENMARK
Olsen, Helle Birk, Allerod, DENMARK

Thim, Lars, Gentofte, DENMARK Bjorn, Soren Erik, Lyngby, DENMARK

APPLICATION INFO.: RELATED APPLN. INFO.:

US 2003-730215 A1 20031208 (10)

Continuation of Ser. No. US 2001-908534, filed on 18 Jul 2001, PENDING Continuation of Ser. No. US

1999-258187, filed on 25 Feb 1999, ABANDONED

Continuation-in-part of Ser. No. US 1997-922200, filed

49 - - -

on 2 Sep 1997, ABANDONED

| | NUMBER | DATE | |
|-----------------------|----------------|----------|------|
| | | | |
| PRIORITY INFORMATION: | DK 1996-931 | 19960830 | |
| | DK 1996-1259 | 19961108 | |
| | DK 1998-271 | 19980227 | |
| | US 1997-35905P | 19970124 | (60) |
| | US 1997-36226P | 19970125 | (60) |
| | US 1998-85789P | 19980518 | (60) |
| DOCUMENT TYPE: | Utility | | |
| FILE SEGMENT. | APPLICATION | | |

Harle 10/042746 Page 41

NOVO NORDISK PHARMACEUTICALS, INC, 100 COLLEGE ROAD LEGAL REPRESENTATIVE:

WEST, PRINCETON, NY, 08540

NUMBER OF CLAIMS: 11 EXEMPLARY CLAIM: 1 LINE COUNT: 1136

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Analogs of GLP-2, pharmaceutical compositions comprising GLP-2 analogs, and methods of treating diseases and disorders comprising administering

such analogs or compositions are provided.

IT 99120-49-7DP, Glucagon-related peptide II (human), derivs.

204319-64-2DP, 1-31-Glucagon-related peptide II (human), derivs. 204401-90-1DP, 1-32-Glucagon-related peptide II (human), derivs.

204401-91-2P 204401-92-3P 204401-93-4P 204401-94-5P 204401-95-6P 204401-96-7P 204401-97-8P 204401-98-9P 204401-99-0P 204402-00-6P 204402-01-7P 204402-02-8P 204402-03-9P 204402-04-0P 204402-05-1P 204402-06-2P 204402-07-3P 204402-08-4P 204402-09-5P 204402-10-8P 204461-70-1P

(preparation of lipophilic derivs. of hGLP-2) IT 99120-49-7, Glucagon-related peptide II (human) (preparation of lipophilic derivs. of hGLP-2)

L46 ANSWER 28 OF 38 USPATFULL on STN

2004:159406 USPATFULL ACCESSION NUMBER:

GLP-2 compounds, formulations, and uses thereof TITLE:

Thim, Lars, Gentofte, DENMARK INVENTOR(S):

Bang, Susanne, Bagsvaerd, DENMARK

Schlein, Morten, Copenhagen S., DENMARK

Kaarsholm, Niels Christian, Vanloese, DENMARK

Engelund, Dorthe Kot, Holte, DENMARK Nielsen, Anette Sams, Bagsvaerd, DENMARK

Johansen, Nils Langeland, Copenhagen OE., DENMARK

Madsen, Kjeld, Vaerlose, DENMARK Zundel, Magali, Soeborg, DENMARK

Thygesen, Peter, Copenhagen OE., DENMARK

NUMBER KIND DATE -----US 2004122210 A1 20040624 US 2003-685368 A1 20031014 PATENT INFORMATION: APPLICATION INFO.: A1 20031014 (10)

NUMBER DATE _____ DK 2002-1574 20021014 PRIORITY INFORMATION: DK 2002-1780 DK 2002-1778 20021119 DK 2002-1778 20021119 US 2002-434562P 20021219 (60) US 2002-434560P 20021219 (60) US 2002-420581P 20021023 (60) US 2002-426273P 20021114 (60)

DOCUMENT TYPE: Utility FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: Reza Green, Esq., Novo Nordisk Pharmaceuticals, Inc.,

100 College Road West, Princeton, NJ, 08540

NUMBER OF CLAIMS: 77 EXEMPLARY CLAIM: 1

12 Drawing Page(s)

NUMBER OF DRAWINGS: LINE COUNT:

7463

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The present invention relates to novel human glucagon-like peptide-2 (GLP-2) peptides and human glucagon-like peptide-2 derivatives which have a protracted profile of action as well as polynucleotide constructs

```
encoding such peptides, vectors and host cells comprising and expressing
       the polynucleotide, pharmaceutical compositions, uses and methods of
       treatment.
IT
     223460-79-5, 1-33-Glucagon-like peptide II (human)
        (amino acid sequence; synthesis and production of glucagon-like peptide-2
        (GLP-2) derivs. and, formulations and therapeutic uses thereof)
TT
     682841-20-9P 682841-27-6P 682841-30-1P
      682841-32-3P 682841-35-6P 682841-43-6P
      682841-46-9P 682841-48-1P 682841-51-6P
      682841-53-8P 682841-54-9P 682841-61-8P
      682841-64-1P 682841-66-3P 682841-69-6P
      683750-88-1P 683750-92-7P 683750-94-9P
      683750-95-0P 683750-96-1P 683750-97-2P
      683751-00-0P 683751-01-1P 683751-06-6P
      683751-16-8P 683751-18-0P 683751-19-1P
      683751-20-4P 683751-21-5P 683751-22-6P
      683751-23-7P 683751-24-8P 683751-25-9P
      683751-26-0P 683751-27-1P 683751-28-2P
      683751-29-3P 683751-30-6P 683751-31-7P
      683751-32-8P 683751-33-9P 683751-34-0P
      683751-35-1P 683751-36-2P 683751-37-3P
      683751-38-4P 683751-39-5P 683751-40-8P
      683751-41-9P 683751-47-5P 683751-48-6P
      683751-49-7P 683751-50-0P 683751-51-1P
      683751-52-2P 683751-53-3P 683751-56-6P
      683752-02-5P_683752-05-8P_683752-07-0P
      683752-08-1P 683752-09-2P 683752-10-5P
      683752-11-6P 683752-12-7P 683752-13-8P
      683752-14-9P 683752-15-0P 683752-16-1P
      683752-17-2P 683752-18-3P 683752-19-4P
      683752-20-7P 683752-21-8P 683752-22-9P
      683752-23-0P 683752-24-1P 683752-25-2P
      683752-26-3P 683752-27-4P 683752-28-5P
      683752-29-6P 683752-30-9P 683752-31-0P
      683752-32-1P 683752-33-2P 683752-34-3P
      683752-35-4P 683752-36-5P 683752-37-6P
      683752-38-7P 683752-39-8P 683752-40-1P
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      683752-44-5P 683752-45-6P 683752-48-9P
      683752-67-2P 683752-70-7P 683752-72-9P
     683752-73-0P 683752-74-1P 683752-75-2P
     683752-76-3P 683752-77-4P 683752-78-5P
     683752-79-6P 683752-80-9P 683752-83-2P
     683752-84-3P 683752-85-4P 683752-87-6P
     683752-88-7P 683752-89-8P 683752-90-1P
     683752-91-2P 683752-92-3P 683752-93-4P
     683752-94-5P 683752-95-6P 683752-96-7P
     683752-97-8P 683752-98-9P 683752-99-0P
     683753-00-6P 683753-01-7P 683753-02-8P
     683753-03-9P 683753-04-0P 683753-05-1P
     683753-07-3P 683753-08-4P 683753-09-5P
     683753-10-8P 683753-11-9P 683753-12-0P
     683753-13-1P 683753-14-2P 683753-17-5P
        (synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and,
       formulations and therapeutic uses thereof)
```

AB

Harle 10/042746 Page 43

ACCESSION NUMBER:

2003:294792 USPATFULL

TITLE:

Methods of enhancing functioning of the large

intestine

INVENTOR (S):

Drucker, Daniel J., Ontario, CANADA

PATENT ASSIGNEE(S):

NPS ALLELIX CORPORATION (non-U.S. corporation)

DATE NUMBER KIND -----

PATENT INFORMATION:

US 2003207809 A1 20031106 US 2003-419150 A1 20030421

APPLICATION INFO.:

(10)

RELATED APPLN. INFO.:

Division of Ser. No. US 2000-692238, filed on 20 Oct 2000, GRANTED, Pat. No. US 6586399 Continuation of Ser. No. US 1998-149831, filed on 8 Sep 1998, GRANTED, Pat. No. US 6297214 Continuation-in-part of Ser. No. US

1997-850664, filed on 2 May 1997, ABANDONED

DOCUMENT TYPE:

Utility APPLICATION

FILE SEGMENT: LEGAL REPRESENTATIVE:

Stephen A. Bent, Foley & Lardner, Washington Harbour,

3000 K Street, N.W., Suite 500, Washington, DC,

20007-5143

NUMBER OF CLAIMS:

14

EXEMPLARY CLAIM: NUMBER OF DRAWINGS: 1 5 Drawing Page(s)

LINE COUNT:

903

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB

The invention relates to glucagon-related peptides and their use for the prevention or treatment of disorders involving the large intestine. In particular, it has now been demonstrated that GLP-2 and peptidic agonists of GLP-2 can cause proliferation of the tissue of large intestine. Thus, the invention provides methods of proliferating the large intestine in a subject in need thereof. Further, the methods of the invention are useful to treat or prevent inflammatory conditions of the large intestine, including inflammatory bowel diseases.

195262-56-7 197664-29-2 197922-42-2 IT 197922-60-4 197923-49-2

(GLP-2 and its analogs for the treatment or prevention of inflammatory conditions of the large intestine)

L46 ANSWER 30 OF 38 USPATFULL on STN

ACCESSION NUMBER:

2003:283328 USPATFULL

TITLE:

Derivatives of GLP-1 analogs

INVENTOR(S):

Knudsen, Liselotte Bjerre, Valby, DENMARK Huusfeldt, Per Olaf, Kobenhavn K, DENMARK Nielsen, Per Franklin, Vaerlose, DENMARK Kaarsholm, Niels C., Vanlose, DENMARK Olsen, Helle Birk, Allerod, DENMARK Bjorn, Soren Erik, Lyngby, DENMARK

Pedersen, Freddy Zimmerdahl, Vaerlose, DENMARK

Madsen, Kjeld, Vaerlose, DENMARK

NUMBER KIND DATE -----A1 20031023 US 2003199672

PATENT INFORMATION: APPLICATION INFO.: RELATED APPLN. INFO.:

US 2002-285079 A1 20020819 (10) Continuation of Ser. No. US 1999-398111, filed on 16

Sep 1999, GRANTED, Pat. No. US 6458924

Continuation-in-part of Ser. No. US 1999-265141, filed

on 8 Mar 1999, GRANTED, Pat. No. US 6384016

Continuation-in-part of Ser. No. US 1999-258750, filed

on 26 Feb 1999, GRANTED, Pat. No. US 6268343 Continuation-in-part of Ser. No. US 1998-38432, filed on 11 Mar 1998, ABANDONED Continuation-in-part of Ser. No. US 1997-918810, filed on 26 Aug 1997, ABANDONED Continuation-in-part of Ser. No. WO 1997-DK340, filed on 22 Aug 1997, UNKNOWN

| | NUMBER | DATE | |
|---|---|--|--|
| PRIORITY INFORMATION: | DK 1996-931 DK 1996-1259 DK 1996-1470 DK 1998-263 DK 1998-264 DK 1998-268 EP 1998-610006 DK 1998-507 DK 1998-272 DK 1998-274 DK 1998-508 DK 1998-509 US 1997-35904P US 1997-36226P US 1997-36255P | 19960830 19961108 19961220 19980227 19980227 19980227 19980313 19980408 19980227 19980227 19980408 19980408 | 0) |
| DOCUMENT TYPE: | Utility | 222.0221 (0 | · . |
| FILE SEGMENT: LEGAL REPRESENTAȚIVE: | | | of North America, Inc., ue, New York, NY, |
| NUMBER OF CLAIMS: | 238 | | |
| EXEMPLARY CLAIM: NUMBER OF DRAWINGS: LINE COUNT: CAS INDEXING IS AVAILAB AB The present inve | 1 Drawing Page(s) 19138 LE FOR THIS PATENT ntion relates to a | pharmaceutic | al composition comprising ent; and a surfactant. |
| 204401-90-1DP, 1- 204401-91-2P 2044 204401-94-5P 2044 204401-97-8P 2044 204402-00-6P 2044 204402-03-9P 2044 204402-06-2P 2044 204402-09-5P 2044 (preparation of | 31-Glucagon-relate 32-Glucagon-relate 01-92-3P 204401-93 01-95-6P 204401-99 01-98-9P 204401-99 02-01-7P 204402-02 02-04-0P 204402-05 02-07-3P 204461-70 lipophilic derivs | d peptide II d peptide II d-4P d-7P d-0P d-8P d-1P d-4P d-1P d-1P d-1P d-1P d-1P d-1P | (human), derivs. |
| IT 99120-49-7 , Glucage (preparation of | on-related peptide lipophilic derive | | |
| L46 ANSWER 31 OF 38 U ACCESSION NUMBER: TITLE: INVENTOR(S): | SPATFULL on STN 2003:57912 USPAT Chemotherapy trea Drucker, Daniel S Boushey, Robin P, | itment , Toronto, CA | |
| | NUMBER | KIND DATE | |
| PATENT INFORMATION: | US 2003040478 | A1 200302 | 27 |

A1

20020722

20001208

(10)

US 2002-148682

WO 2000-IB2003

APPLICATION INFO.:

Harle 10/042746

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: FOLEY AND LARDNER, SUITE 500, 3000 K STREET NW,

WASHINGTON, DC, 20007

NUMBER OF CLAIMS: 21 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 10 Drawing Page(s)

LINE COUNT: 923

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

This invention provides a treatment regimen that is effective in inhibiting chemotherapy-induced apoptosis and promoting cell survival. The invention also relates to a treatment regimen that confers resistance to caspase activation, thereby inhibiting caspase-mediated, proteolytic cleavage of functional cellular enzymes. Specifically, subjects undergoing chemotherapy are first exposed to a pretreatment regimen. Under this regimen, a GLP-2 receptor activator, such as h[GLY2]-GLP2, is administered each day for a predetermined beneficial period, e.g., three consecutive days. Approximately about 1 week following pretreatment, the subjects are exposed to an appropriate chemotherapy treatment regimen. Pretreatment with a GLP-2 receptor activator followed by administration of chemotherapeutic agents improves cell survival, reduces bacteremia, attenuates epithelial injury, and inhibits cellular apoptosis. Moreover, it does not impair the effectiveness of chemotherapy nor result in weight loss. The anti-apoptotic effects of GLP-2 may be useful in the reduction of cytoxicity and bacterial infection induced by chemotherapeutic agents.

IT 197922-42-2

(treatment with h[Gly2]-GLP-2 to attenuate cancer chemotherapy-induced adverse apoptosis and to promote cell survival)

L46 ANSWER 32 OF 38 USPATFULL on STN

ACCESSION NUMBER: 2003:176402 USPATFULL

TITLE: Methods of enhancing functioning of the large

intestine

INVENTOR(S): Drucker, Daniel J., Ontario, CANADA

PATENT ASSIGNEE(S): 1149336 Ontario, Inc., Toronto, CANADA (non-U.S.

corporation)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1998-149831, filed on 8 Sep.

1998, now patented, Pat. No. US 6297214

Continuation-in-part of Ser. No. US 1997-850664, filed

on 2 May 1997, now abandoned

DOCUMENT TYPE: Utility FILE SEGMENT: GRANTED

PRIMARY EXAMINER: Low, Christopher S. F.

ASSISTANT EXAMINER: Kam, Chih-Min LEGAL REPRESENTATIVE: Foley & Lardner

NUMBER OF CLAIMS: 16 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 8 Drawing Figure(s); 5 Drawing Page(s)

LINE COUNT: 899

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The invention relates to glucagon-related peptides and their use for the prevention or treatment of disorders involving the large intestine. In particular, it has now been demonstrated that GLP-2 and peptidic agonists of GLP-2 can cause proliferation of the tissue of large intestine. Thus, the invention provides

US

America, Inc.,

10/042746 Harle

methods of proliferating the large intestine in a subject in need thereof. Further, the methods of the invention are useful to treat or prevent inflammatory conditions of the large intestine, including inflammatory bowel diseases.

195262-56-7 197664-29-2 197922-42-2 TT 197922-60-4 197923-49-2

(GLP-2 and its analogs for the treatment or prevention of inflammatory conditions of the large intestine)

L46 ANSWER 33 OF 38 USPATFULL on STN

ACCESSION NUMBER:

2002:43566 USPATFULL

TITLE:

GLP-2 derivatives

INVENTOR(S):

Knudsen, Liselotte Bjerre, Valby, DENMARK Huusfeldt, Per Olaf, Kobenhavn K, DENMARK Nielsen, Per Franklin, Vaerlose, DENMARK Kaarsholm, Niels C., Vanlose, DENMARK Olsen, Helle Birk, Allerod, DENMARK Thim, Lars, Gentofte, DENMARK

Bjorn, Soren Erik, Lyngby, DENMARK

| | NUMBER | KIND | DATE | | | | | |
|-----------------------|--|----------|------------|---------------------|--|--|--|--|
| | | | | | | | | |
| PATENT INFORMATION: | US 2002025933 | | 20020228 | | | | | |
| APPLICATION INFO .: | US 2001-908534 | | | | | | | |
| RELATED APPLN. INFO.: | Continuation of | Ser. No | . US 1999- | 258187, filed on 25 | | | | |
| | Feb 1999, ABANDONED Continuation-in-part of Ser. No. | | | | | | | |
| | 1997-922200, fil | led on 2 | Sep 1997, | ABANDONED | | | | |

| | NUMBER | DATE | |
|-----------------------|--|-----------------------------------|---------------------------------------|
| | | | |
| PRIORITY INFORMATION: | DK 1996-931 | 19960830 | |
| | DK 1996-1259 | 19961108 | |
| | DK 1998-271 | 19980227 | |
| | US 1997-35905P | 19970124 (60) | |
| | US 1997-36226P | 19970125 (60) | |
| | US 1998-85789P | 19980518 (60) | |
| DOCUMENT TYPE: | Utility | | |
| FILE SEGMENT: | APPLICATION | | • |
| LEGAL REPRESENTATIVE: | Reza Green, Esq., Suite 6400, 405 L | Novo Nordisk o exington Avenue | of North America, e, New York, NY, |

10174-6401 57 NUMBER OF CLAIMS: EXEMPLARY CLAIM: 7 877 LINE COUNT:

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The present invention relates to derivatives of hGLP-2 and analogues and/or fragments thereof having a lipophilic substituent have interesting pharmacological properties, in particular they have a more protracted profile of action than the parent peptides.

```
99120-49-7DP, Glucagon-related peptide II (human), derivs.
IT
      204319-64-2DP, 1-31-Glucagon-related peptide II (human), derivs.
      204401-90-1DP, 1-32-Glucagon-related peptide II (human), derivs.
      204401-91-2P 204401-92-3P 204401-93-4P
      204401-94-5P 204401-95-6P 204401-96-7P
      204401-97-8P 204401-98-9P 204401-99-0P
      204402-00-6P 204402-01-7P 204402-02-8P
      204402-03-9P 204402-04-0P 204402-05-1P
      204402-06-2P 204402-07-3P 204402-08-4P
      204402-09-5P 204402-10-8P 204461-70-1P
        (preparation of lipophilic derivs.
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of hGLP-2)
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99120-49-7, Glucagon-related peptide II (human) IT (preparation of lipophilic derivs. of hGLP-2)

L46 ANSWER 34 OF 38 USPATFULL on STN

ACCESSION NUMBER:

2002:102478 USPATFULL

TITLE:

Stabilized aqueous peptide solutions

INVENTOR(S): PATENT ASSIGNEE(S): Kaarsholm, Niels C., Vanl.o slashed.se, DENMARK Novo Nordisk A/S, Bagsvaerd, DENMARK (non-U.S.

corporation)

KIND DATE NUMBER -----PATENT INFORMATION:

APPLICATION INFO.:

US 6384016 B1 20020507 US 1999-265141 19990308 19990308 (9)

NUMBER DATE -----

PRIORITY INFORMATION:

EP 1998-610006 19980313 US 1998-78422P 19980318 (60)

DOCUMENT TYPE: Utility FILE SEGMENT: GRANTED

PRIMARY EXAMINER:

PRIMARY EXAMINER: Low, Christopher S. F. ASSISTANT EXAMINER: Mohamed, Abdel A.

LEGAL REPRESENTATIVE: Green, Esq., Reza, Gregg, Esq., Valeta A.

NUMBER OF CLAIMS: EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 7 Drawing Figure(s); 7 Drawing Page(s)

LINE COUNT: 490

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Aqueous compositions comprising at least one peptide selected from glucagon, GLP-1, and analogues and derivatives thereof together with a stabilizing and solubilizing amount of at least one detergent, said detergent having at least 2 positive charges, at least 2 negative charges, or a combination of at least one positive charge and at least one negative charge.

IT 99120-49-7DP, Glucagon-related peptide II (human), derivs.

204319-64-2DP, 1-31-Glucagon-related peptide II (human), derivs. 204401-90-1DP, 1-32-Glucagon-related peptide II (human), derivs.

204401-91-2P 204401-92-3P 204401-93-4P 204401-94-5P 204401-95-6P 204401-96-7P 204401-97-8P 204401-98-9P 204401-99-0P 204402-00-6P 204402-01-7P 204402-02-8P 204402-03-9P 204402-04-0P 204402-05-1P

204402-06-2P 204402-07-3P 204402-08-4P

204402-09-5P 204402-10-8P 204461-70-1P

(preparation of lipophilic derivs. of hGLP-2) IT 99120-49-7, Glucagon-related peptide II (human) (preparation of lipophilic derivs. of hGLP-2)

L46 ANSWER 35 OF 38 USPATFULL on STN

ACCESSION NUMBER: 2001:218592 USPATFULL TITLE: Extendin derivatives

INVENTOR(S): Knudsen, Liselotte Bjerre, Valby, Denmark

> Huusfeldt, Per Olaf, Copenhagen K, Denmark Nielsen, Per Franklin, Vaerlose, Denmark

Madsen, Kjeld, Vaerlose, Denmark

KIND DATE NUMBER -----

PATENT INFORMATION: US 2001047084 A1 20011129 Harle 10/042746 Page 48

APPLICATION INFO.: US 2001-886311 A1 20010621 (9)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1999-312177, filed on 14

May 1999, ABANDONED Continuation of Ser. No. WO

1999-DK86, filed on 24 Feb 1999, UNKNOWN

NUMBER DATE

PRIORITY INFORMATION: DK 1998-274 19980227

US 1998-84357P 19980505 (60)

DOCUMENT TYPE: Utility

FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Reza Green, Esq., Novo Nordisk of North America, Inc.,

Suite 6400, 405 Lexington Avenue, New York, NY,

10174-6401

NUMBER OF CLAIMS: 91 EXEMPLARY CLAIM: 1 LINE COUNT: 2488

IT

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to a derivative of GLP-1 (7-C), wherein C is 35 or 36 which derivative has just one lipophilic substituent which

is attached to the C-terminal amino acid residue.

IT 99120-49-7DP, Glucagon-related peptide II (human), derivs.

204319-64-2DP, 1-31-Glucagon-related peptide II (human), derivs.

204401-90-1DP, 1-32-Glucagon-related peptide II (human), derivs.

204401-91-2P 204401-92-3P 204401-93-4P 204401-94-5P 204401-95-6P 204401-96-7P 204401-97-8P 204401-98-9P 204401-99-0P 204402-00-6P 204402-01-7P 204402-02-8P 204402-03-9P 204402-04-0P 204402-05-1P

204402-06-2P 204402-07-3P 204402-08-4P 204402-09-5P 204402-10-8P 204461-70-1P

(preparation of lipophilic derivs. of hGLP-2) 99120-49-7, Glucagon-related peptide II (human)

(preparation of lipophilic derivs. of hGLP-2)

L46 ANSWER 36 OF 38 USPATFULL on STN

ACCESSION NUMBER: 2001:168091 USPATFULL

TITLE: Photochemical singlet oxygen generations having

TITLE: Photochemical singlet oxygen generations having

enhanced singlet oxygen yields

INVENTOR(S): Willey, Alan David, Cincinnati, OH, United States

Harriman, Anthony, Bischheim, France Jeffreys, Brian, Grimbergen, Belgium

Ingram, David William, Woluwe Saint-Lambergt, Belgium

PATENT ASSIGNEE(S): Case Western Reserve University, Cleveland, OH, United

States (U.S. corporation)

19990723 PCT 371 date 19990723 PCT 102(e) date

NUMBER DATE

PRIORITY INFORMATION: US 1997-35904P 19970124 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Hardee, John

Harle 10/042746

Page 49

LEGAL REPRESENTATIVE: Fay Sharpe Fagan Minnich & McKee, LLP

NUMBER OF CLAIMS: 15 EXEMPLARY CLAIM: 1 LINE COUNT: 1743

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The invention relates to photochemical singlet oxygen generators useful as bleaching agents or anti-microbial agents in laundry detergent compositions or in hard surface cleaning compositions. The singlet oxygen generators described herein have enhanced singlet oxygen generation due to aromatic moieties teed to the molecules, said aromatic moieties absorbing ultra violet radiation then re-emitting the radiation as fluorescence at a wavelength absorbable by the singlet oxygen producing photosensitizer unit. The increase in the number of photons having an absorbable wavelength provides an increase in the production of singlet oxygen.

(preparation of lipophilic derivs. of hGLP-2)

L46 ANSWER 37 OF 38 USPATFULL on STN

ACCESSION NUMBER: 2000:47214 USPATFULL

TITLE: Methods of enhancing functioning of the upper

gastrointestinal tract

INVENTOR(S): Drucker, Daniel J., Ontario, Canada

PATENT ASSIGNEE(S): 1149336 Ontario Inc., Toronto, Canada (non-U.S.

corporation)

NUMBER DATE

PRIORITY INFORMATION: US 1997-46754P 19970516 (60)

DOCUMENT TYPE: Utility FILE SEGMENT: Granted

PRIMARY EXAMINER: Tsang, Cecilia J.
ASSISTANT EXAMINER: Delacroix-Muirheid, C.
LEGAL REPRESENTATIVE: Pennie & Edmonds LLP

NUMBER OF CLAIMS: 48 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 3 Drawing Figure(s); 2 Drawing Page(s)

LINE COUNT: 1847

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to glucagon-related peptides and their use for the prevention or treatment of disorders involving the upper gastrointestinal tract including the esophagus and stomach. In particular, it has now been demonstrated that GLP-2

and peptidic agonists of GLP-2 can cause proliferation of the tissue of

the upper gastrointestinal tract. Thus, the invention provides methods of proliferating the upper gastrointestinal tract in a subject in need thereof. Further, the methods of the invention are useful to treat or prevent inflammatory conditions of the upper gastrointestinal tract, including inflammatory diseases. GLP-2 stimulates the growth of upper gastrointestinal tissue when administered in conjunction with other peptide hormones. The invention further provides pharmaceutical compositions of GLP-2 with at least one other peptide hormone, methods of enhancing the growth of upper gastrointestinal tissue and of gastrointestinal disorders by increasing serum levels of GLP-2 and at least one other peptide hormone, and kits for preforming the methods of the invention.

IT 197922-42-2

(glucagon-like peptide 2 formulations for enhancing functioning of the upper gastrointestinal tract)

L46 ANSWER 38 OF 38 USPATFULL on STN

ACCESSION NUMBER: 1999:151180 USPATFULL

TITLE: Glucagon-like peptide-2 and its therapeutic use

INVENTOR(S): Drucker, Daniel J., Toronto, Canada

PATENT ASSIGNEE(S): 1149336 Ontario Inc., Toronto, Canada (non-U.S.

corporation)

NUMBER KIND DATE

PATENT INFORMATION: US 5990077 19991123

APPLICATION INFO.: US 1995-422540 19950414 (8)

DOCUMENT TYPE: Utility

FILE SEGMENT: Granted

PRIMARY EXAMINER: Huff, Sheela

LEGAL REPRESENTATIVE: Pennie & Edmonds LLP

NUMBER OF CLAIMS: 80
EXEMPLARY CLAIM: 1
LINE COUNT: 1128

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Glucagon-like peptide 2, a product of glucagon gene expression, has been identified as a **gastrointestinal** tissue growth factor. Its effects on the growth of small **intestine** and on pancreatic islets are described. Its formulation as a pharmaceutical, and its therapeutic use in treating bowel tissue disorders and in treating diabetes, are described.

=> => fil cancer medl; d que 165
FILE=CANCERLIT' ENTERED AT 16:50:27 ON 27 DEC 2004

FILE MEDLINE' ENTERED AT 16:50:27 ON 27 DEC 2004

```
290 SEA GLUCAGON-LIKE PEPTIDE 2 OR GLP2 OR GLP 2
L53
          2369 SEA PEPTIDES/CT(L) TU/CT - Subherding Tu = therapertic use
L54
        58573 SEA PEPTIC ULCER+NT/CT
L55
        20646 SEA MALABSORPTION SYNDROMES+NT/CT
L56
        37686 SEA INFLAMMATORY BOWEL DISEASES+NT/CT
10057 SEA CELIAC DISEASE/CT
L57
L58
         435 SEA SPRUE, TROPICAL/CT
L59
Peo.
         4866 SEA AGAMMAGLOBULINEMIA/CT
L61
         7976 SEA ENTERITIS+NT/CT
L62
         1498 SEA SHORT BOWEL SYNDROME/CT
         1135 SEA DIGESTI? (3A) DISORDER?
L63
         1189 SEA SHORT GUT OR CUL DE SAC
L64
L'65_____19_SEA_L53_AND_L54_AND_(L55_OR_L56_OR_L57_OR_L58_OR_L59_OR_L60_OR_,
               L61_OR_L62_OR_L63_OR_L64)___
```

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L53
290 SEA GLUCAGON-LIKE PEPTIDE 2 OR GLP2 OR GLP 2
L54
2369 SEA PEPTIDES/CT(L) TU/CT
L69
6833 SEA INTESTINES+NT/CT(L) TR/CT - Subheading TR = transplantation
L70
2 SEA L69-AND-L53-AND-L54
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L53 290 SEA GLUCAGON-LIKE PEPTIDE 2 OR GLP2 OR GLP 2
L54 2369 SEA PEPTIDES/CT(L) TU/CT
L74 127216 SEA DIABETES MELLITUS+NT/CT
L75 1 SEA L74 AND L53 AND L54 14
```

=> s 165 or 170 or 175; fil embase; d que 192; d que 195; s 192 or 195

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FILE COVERS 1974 TO 17 Dec 2004 (20041217/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

L76 181 SEA FILE=EMBASE ABB=ON GLUCAGON LIKE PEPTIDE 2/CT OR GLUCAGON LIKE PEPTIDE 2 DERIVATIVE/CT

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44948 SEA FILE=EMBASE ABB=ON PEPTIC ULCER+NT/CT
L77
          17635 SEA FILE=EMBASE ABB=ON MALABSORPTION+NT/CT
L78
          62623 SEA FILE=EMBASE ABB=ON ENTERITIS+NT/CT
L79
          18146 SEA FILE=EMBASE ABB=ON CROHN DISEASE/CT
L80
          6872 SEA FILE=EMBASE ABB=ON CELIAC DISEASE/CT
L81
           1781 SEA FILE=EMBASE ABB=ON HYPOGAMMAGLOBULINEMIA/CT
L82
             13 SEA FILE=EMBASE ABB=ON CUL DE SAC/CT OR CUL DE SAC DISEASE/CT
L83
         177035 SEA FILE=EMBASE ABB=ON DIGESTIVE SYSTEM FUNCTION DISORDER+NT/C
L84
                т
           8260 SEA FILE=EMBASE ABB=ON PANCREAS ISLET/CT
L85
         171074 SEA FILE=EMBASE ABB=ON DIABETES MELLITUS+NT/CT
L86
           2741 SEA FILE=EMBASE ABB=ON INTESTINE GRAFT/CT OR INTESTINE
L87
                TRANSPLANTATION/CT
L89
             28 SEA FILE=EMBASE ABB=ON L76(L)DT/CT
             14 SEA FILE=EMBASE ABB=ON L89/MAJ
L91
L92-
             -10_SEA_FILE=EMBASE_ABB=ON-L91-AND-(L77_OR_L78_OR_L79_OR_L80=OR \
                L81-OR-L82-OR-L83-OR-L84-OR-L85-OR-L86-OR-L87)
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181 SEA FILE=EMBASE ABB=ON GLUCAGON LIKE PEPTIDE 2/CT OR GLUCAGON
L76
                LIKE PEPTIDE 2 DERIVATIVE/CT
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L77
          17635 SEA FILE=EMBASE ABB=ON MALABSORPTION+NT/CT
L78
          62623 SEA FILE=EMBASE ABB=ON ENTERITIS+NT/CT
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L81
           6872 SEA FILE=EMBASE ABB=ON CELIAC DISEASE/CT
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L82
             13 SEA FILE=EMBASE ABB=ON CUL DE SAC/CT OR CUL DE SAC DISEASE/CT
L83
         177035 SEA FILE=EMBASE ABB=ON DIGESTIVE SYSTEM FUNCTION DISORDER+NT/C
L84
                Т
L85
           8260 SEA FILE=EMBASE ABB=ON PANCREAS ISLET/CT
         171074 SEA FILE=EMBASE ABB=ON DIABETES MELLITUS+NT/CT
L86
           2741 SEA FILE=EMBASE ABB=ON INTESTINE GRAFT/CT OR INTESTINE
L87
                TRANSPLANTATION/CT
             64 SEA FILE=EMBASE ABB=ON L76(L)EC/CT EC = endo alnows compound
76 SEA FILE=EMBASE ABB=ON L76/MAJ NOT L93
L93
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L94
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L9.5
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FILE 'MEDLINE' ENTERED AT 16:51:02 ON 27 DEC 2004

FILE 'EMBASE' ENTERED AT 16:51:02 ON 27 DEC 2004
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PROCESSING COMPLETED FOR L97
PROCESSING COMPLETED FOR L98
(11 DUPLICATES REMOVED)

ANSWERS '1-5' FROM FILE CANCERLIT
ANSWERS '6-15' FROM FILE MEDLINE
ANSWERS '16-35' FROM FILE EMBASE

<=>_d_iall_1=35; fil hom

Harle 10/042746 Page 53

L99 ANSWER 1 OF 35 CANCERLIT on STN DUPLICATE 5

ACCESSION NUMBER: 2002121279 CANCERLIT

DOCUMENT NUMBER: 21593333 PubMed ID: 11757811

TITLE: Enhancement of intestinal growth and repair by growth

factors.

AUTHOR: Howarth G S; Shoubridge C A

CORPORATE SOURCE: Child Health Research Institute, North Adelaide, South

Australia.. gordon.howarth@adelaide.edu.au

SOURCE: Curr Opin Pharmacol, (2001 Dec) 1 (6) 568-74. Ref: 58

Journal code: 100966133. ISSN: 1471-4892.

PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

(REVIEW LITERATURE)

LANGUAGE: English

FILE SEGMENT: MEDLINE; Priority Journals

OTHER SOURCE: MEDLINE 2002031826

ENTRY MONTH: 200203

ENTRY DATE: Entered STN: 20020726

Last Updated on STN: 20020726

ABSTRACT:

Recently, glucagon-like peptide 2 has

emerged as a potent stimulator of epithelial growth, joining insulin-like growth factor I, hepatocyte growth factor and keratinocyte growth factor as potential treatment modalities for intestinal disorders associated with loss of mucosal mass, such as short bowel syndrome. Investigations into other members of the expanded epidermal growth factor peptide family, the development of more potent peptide analogues, and advances in the development of enterally administered bioactive growth factor formulations further expands the repertoire of epithelial growth factors applicable to conditions associated with epithelial insufficiency.

CONTROLLED TERM: Check Tags: Human

Adaptation, Physiological

Epidermal Growth Factor: PH, physiology Fibroblast Growth Factors: PH, physiology Fibroblast Growth Factors: TU, therapeutic

Fibroblast Growth Factors: TU, therapeutic use *Growth Substances: PH, physiology

Growth Substances: TH, physiology
Hepatocyte Growth Factor: PH, physiology
Hepatocyte Growth Factor: TU, therapeutic use

Intestinal Diseases: DT, drug therapy
*Intestinal Diseases: PA, pathology
*Intestinal Mucosa: PA, pathology

Peptides: PH, physiology

Peptides: TU, therapeutic use

Regeneration

Short Bowel Syndrome: DT, drug therapy Short Bowel Syndrome: PA, pathology

Somatomedins: PH, physiology Somatomedins: TU, therapeutic use

Transforming Growth Factor alpha: PH, physiology

CAS REGISTRY NO.: 126469-10-1 (keratinocyte growth factor); 146046-78-8

(trefoil factor); 62031-54-3 (Fibroblast Growth Factors);

62229-50-9 (Epidermal Growth Factor); 67256-21-7 (Hepatocyte Growth Factor); 82905-30-4 (glucagon-like-

immunoreactivity)

CHEMICAL NAME: 0 (Growth Substances); 0 (Peptides); 0 (Somatomedins); 0

(Transforming Growth Factor alpha)

L99 ANSWER 2 OF 35 CANCERLIT on STN DUPLICATE 6

ACCESSION NUMBER: 2002134682 CANCERLIT

Harle 10/042746

DOCUMENT NUMBER: 21562522 PubMed ID: 11706294 TITLE: Treatment of short-bowel syndrome.

AUTHOR:

Scolapio J S

CORPORATE SOURCE:

Division of Gastroenterology, Mayo Clinic, Jacksonville,

Florida 32224, USA.. scolapio.james@mayo.edu

SOURCE:

CURRENT OPINION IN CLINICAL NUTRITION AND METABOLIC CARE,

(2001 Nov) 4 (6) 557-60. Ref: 41

Journal code: 9804399. ISSN: 1363-1950.

PUB. COUNTRY:

England: United Kingdom

DOCUMENT TYPE:

Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

(REVIEW, TUTORIAL)

LANGUAGE:

English

FILE SEGMENT:

MEDLINE; Priority Journals

OTHER SOURCE:

MEDLINE 2001653063

ENTRY MONTH:

200204

ENTRY DATE:

Entered STN: 20020726

Last Updated on STN: 20020726

ABSTRACT:

The present article reviews the current literature on the role of diet and other trophic factors in the treatment of short-bowel syndrome. Results using glutamine, growth hormone and glucagon-like peptide

2 are reviewed. Although experimental animal data would suggest that various growth factors are of benefit in the treatment of short-bowel syndrome, only a few clinical studies have made the same claim.

CONTROLLED TERM:

Check Tags: Animal; Human

Colon: PH, physiology

Dietary Carbohydrates: AD, administration & dosage

Dietary Carbohydrates: CL, classification

Disease Models, Animal-

Glutamine: TU, therapeutic use

Growth Substances: TU, therapeutic use Intestine, Small: TR, transplantation

Peptides: TU, therapeutic use

Short Bowel Syndrome: DH, diet therapy

Short Bowel Syndrome: SU, surgery *Short Bowel Syndrome: TH, therapy

CAS REGISTRY NO.:

56-85-9 (Glutamine); 82905-30-4 (glucagon-like-

immunoreactivity)

CHEMICAL NAME:

0 (Dietary Carbohydrates); 0 (Growth Substances); 0

(Peptides)

L99 ANSWER 3 OF 35 CANCERLIT on STN

DUPLICATE 8

ACCESSION NUMBER: DOCUMENT NUMBER:

2000329425

CANCERLIT 20329425 PubMed ID: 10873024

TITLE:

Treatment of inflammatory bowel disease in a rodent model

with the intestinal growth factor glucagon-

like peptide-2.

AUTHOR:

Alavi K; Schwartz M Z; Palazzo J P; Prasad R

CORPORATE SOURCE:

Department of Surgery, AI duPont Hospital for Children,

Wilmington, Delaware 19803, USA.

SOURCE:

JOURNAL OF PEDIATRIC SURGERY, (2000 Jun) 35 (6) 847-51.

Journal code: 0052631. ISSN: 0022-3468.

PUB. COUNTRY:

United States

DOCUMENT TYPE:

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE:

English

FILE SEGMENT:

MEDLINE; Priority Journals

OTHER SOURCE:

MEDLINE 2000496614

ENTRY MONTH:

200010

ENTRY DATE:

Entered STN: 20001128

Last Updated on STN: 20001128

and then released from enteroendocrine cells in the small and large intestine. GLP-1 promotes efficient nutrient assimilation while GLP-2 regulates energy absorption via effects on nutrient intake, gastric acid secretion and gastric emptying, nutrient absorption, and mucosal permeability. Preliminary human studies indicate that GLP-2 may enhance energy absorption and reduce fluid loss in subjects with short bowel syndrome suggesting that GLP-2 functions as a key regulator of mucosal integrity, permeability, and nutrient absorption. Hence GLPmay be therapeutically useful in diseases characterised by injury or dysfunction of the gastrointestinal epithelium. CONTROLLED TERM: Check Tags: Human; Support, Non-U.S. Gov't *Adaptation, Physiological: PH, physiology Animals Glucagon: PH, physiology Intestinal Diseases: DT, drug therapy *Intestines: PH, physiology Mice Peptide Fragments: PH, physiology *Peptides: PH, physiology Peptides: TU, therapeutic use Protein Precursors: PH, physiology Short Bowel Syndrome: DT, drug therapy CAS REGISTRY NO.: 82905-30-4 (glucagon-like-immunoreactivity); 89750-14-1 (glucagon-like peptide 1); 9007-92-5 (Glucagon) CHEMICAL NAME: 0 (Peptide Fragments); 0 (Peptides); 0 (Protein Precursors) L99 ANSWER 12 OF 35 MEDLINE on STN ACCESSION NUMBER: 2001216596 MEDLINE DOCUMENT NUMBER: PubMed ID: 11231959 TITLE: GLP-2 as therapy for the short-bowel syndrome. Comment on: Gastroenterology. 2001 Mar; 120(4):806-15. COMMENT: PubMed ID: 11231933 AUTHOR: Warner B W Gastroenterology, (2001 Mar) 120 (4) 1041-3. Ref: 23 SOURCE: Journal code: 0374630. ISSN: 0016-5085. PUB. COUNTRY: United States DOCUMENT TYPE: Commentary Editorial General Review; (REVIEW) (REVIEW, TUTORIAL) LANGUAGE: English Abridged Index Medicus Journals; Priority Journals FILE SEGMENT: ENTRY MONTH: 200104 ENTRY DATE: Entered STN: 20010425 Last Updated on STN: 20010425 Entered Medline: 20010419 CONTROLLED TERM: Check Tags: Human *Peptides: TU, therapeutic use *Short Bowel Syndrome: DT, drug therapy 82905-30-4 (glucagon-like-immunoreactivity) CAS REGISTRY NO.: CHEMICAL NAME: 0 (Peptides) L99 ANSWER 13 OF 35 MEDLINE on STN ACCESSION NUMBER: 2001179482 MEDLINE DOCUMENT NUMBER: PubMed ID: 11159819 Minireview: the glucagon-like peptides. TITLE: AUTHOR: Drucker D J Department of Medicine, Toronto General Hospital, Banting CORPORATE SOURCE: and Best Diabetes Centre, University of Toronto, Toronto,

Ontario M5G 2C4 Canada.. d.drucker@utoronto.ca

Harle 10/042746 Page 63

ENTRY MONTH:

200112

ENTRY DATE:

Entered STN: 20010924

Last Updated on STN: 20020122 Entered Medline: 20011204

ABSTRACT:

NPS Allelix (formerly Allelix Biopharmaceuticals) is developing the

glucagon -like peptide 2 (GLP-

2) analog ALX-0600 for the potential treatment of gastrointestinal diseases, including short bowel disease. GLP stimulates the growth of the lining of the small intestine, thus increasing the absorptive area of the intestine [214370], [315107]. ALX-0600 also has potential for mucositis associated with cancer chemotherapy and inflammatory bowel disease [331459]. During the third quarter of 1999, a pilot phase II trial began for short bowel syndrome (SBS) [331459]. ALX-0600 began pivotal phase II trials in 2000 following the completion of the pilot trial which was designed to measure the safety, tolerability, and any other drug-related improvements in nutrient absorption and physical changes in the gut of a small number of patients with SBS. Allelix hopes to bring this drug to the market by 2001 [341519]. Allelix filed an application to the FDA for Orphan Drug designation in the third quarter of 1999 [331459]; in August, the designation was approved [377524]. As of November 1998, Allelix was in discussions with a potential marketing partner for worldwide development and marketing [305000]. In August 1998, the USPTO issued a notice of allowance to Allelix for its basic patent containing claims covering the composition and medical uses of ALX-0600 and related GI drug candidate compounds [2946571.

CONTROLLED TERM:

Check Tags: Human

Amino Acid Sequence

Animals

Clinical Trials

*Gastrointestinal Agents: PD, pharmacology *Gastrointestinal Agents: TU, therapeutic use

Molecular Sequence Data Peptides: ME, metabolism *Peptides: PD, pharmacology *Peptides: TU, therapeutic use

*Short Bowel Syndrome: DT, drug therapy

Structure-Activity Relationship

CAS REGISTRY NO.: CHEMICAL NAME:

82905-30-4 (glucagon-like-immunoreactivity)

L99 ANSWER 11 OF 35 MEDLINE on STN

MEDLINE ACCESSION NUMBER: 2002108290

DOCUMENT NUMBER:

PubMed ID: 11839727

TITLE: **AUTHOR:**

SOURCE:

Gut adaptation and the glucagon-like peptides.

CORPORATE SOURCE:

Drucker D J

The Banting and Best Diabetes Centre, Department of Medicine, Toronto General Hospital, University of Toronto,

0 (ALX-0600); 0 (Gastrointestinal Agents); 0 (Peptides)

Toronto, Ontario, Canada M5G 2C4. d.drucker@utoronto.ca Gut, (2002 Mar) 50 (3) 428-35. Ref: 94

Journal code: 2985108R. ISSN: 0017-5749.

PUB. COUNTRY:

England: United Kingdom

DOCUMENT TYPE:

Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

(REVIEW, TUTORIAL)

LANGUAGE:

English

FILE SEGMENT:

Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH:

200203

ENTRY DATE:

Entered STN: 20020213

Last Updated on STN: 20020322 Entered Medline: 20020321

ABSTRACT:

The glucagon-like peptides GLP-1 and GLP-2 are synthesised